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VOL. XXXIII] *SECTION A* [NO. 2

FEBRUARY, 1951

Price Rs. 2 or 3 Sh. *Annual Subscription Rs. 18*

PRINTED AT THE BANGALORE PRESS, BANGALORE CITY, BY G. SRINIVASA RAO,
SUPERINTENDENT, AND PUBLISHED BY THE INDIAN ACADEMY OF SCIENCES,
BANGALORE.

A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part IV. Thiophenes and Thiapyrans from Naphthalene Thiols

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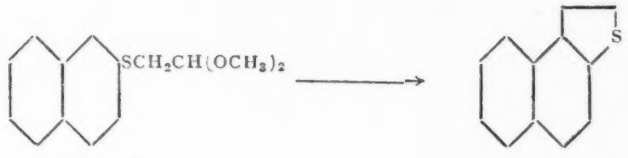
(Department of Chemical Technology, University of Bombay)

Received September 18, 1950

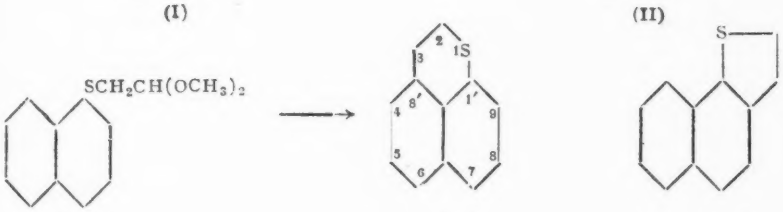
(Communicated by Dr. K. Venkataraman, F.A.SC.)

THE syntheses of thionaphthene and its derivatives from thiophenol and substituted thiophenols have been described in the previous communications.[1] Syntheses of more complex thiophenes and thiapyrans starting from naphthalene mono and dithiols are now described.

β-Naphthyl ω-dimethoxyethyl sulphide (I), obtained by the condensation of β-thionaphthol with bromoacetaldehyde dimethyl acetal, gave 4:5-benzothionaphthene (II) by cyclization in the reactive α-position. The latter compound has been prepared earlier by the reduction of the corresponding 3-hydroxy derivative, which is obtained by the α-ring closure of β-thionaphthoxyacetic acid.[2] An alternative route to (II) consists in the decarboxylation of 4:5-benzothionaphthene-2:3-dicarboxylic acid.[2]



(I) (II)



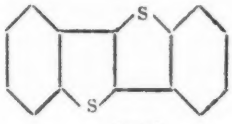
(III) (IV) (V)

Ring-closure of α-naphthyl ω-dimethoxyethyl sulphide (III) gave a product, which being different from 6:7-benzothionaphthene[3] (V), is consti-

tuted as naphtho-(1′ : 8′-*bc*)-thiapyran (IV). An unambiguous synthesis of (V) will be reported separately.[4]

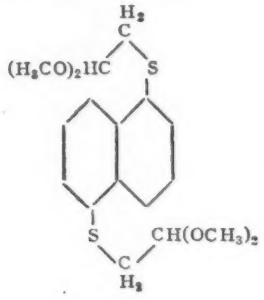
Tetracyclic compounds containing two thiophene or thiapyran rings and two benzene or one naphthalene ring are unknown, with the probable exception of the pyrolysis product of *S*-acetylthiosalicylic acid for which the structures (VI) or (VII) have been suggested.[5] These compounds are of interest as potential carcinogens, *e.g.*, (VI) is the sulphur isoster of the carcinogenic hydrocarbon, 3 : 4-benzophenanthrene. Application of the new synthesis to naphthalene-1 : 5 and 2 : 6-dithiols has led to such tetracyclic compounds.

(VI)

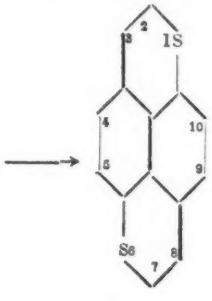


(VII)

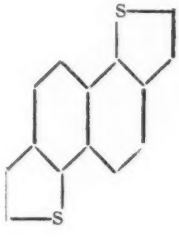
Naphthalene-1 : 5-dithiol was prepared in 85% yield by an improvement of the method of Albenga and Corbellini.[6] Reaction of the dithiol with two molecules of bromoacetaldehyde dimethyl acetal, gave 1 : 5-*bis*-dimethoxyethylmercapto-naphthalene (VIII). On ring-closure, the latter gave an orange-coloured product which is constituted as (IX) and named "1 : 6-dithiapyrene" from its apparent structural similarity to pyrene. Cyclization of (VIII) takes place in the *peri* positions, because β-cyclization would have led to 6 : 7, 7′ : 6′-dithionaphthene (X), an isoster of chrysene (XIII), which would probably be a colourless substance.



(VIII)

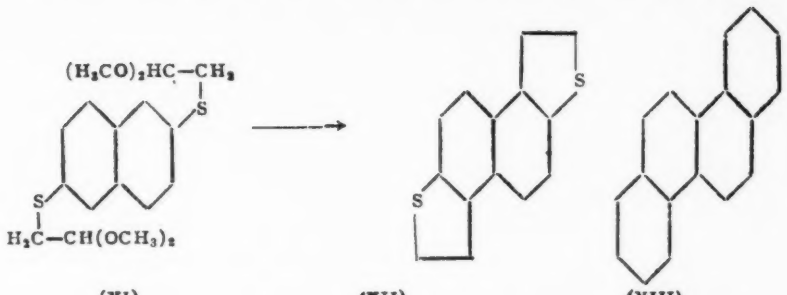


(IX)



(X)

The *peri*-ring-closure of (VIII) to give the orange-coloured compound (IX) is supported by the fact that the sulphur isoster (XII) of chrysene is colourless. 2 : 6-*Bis*-dimethoxyethylmercapto-naphthalene (XI) cyclized in the reactive α-positions to give 4 : 5, 5′ : 4′-dithionaphthene (XII).



(XI) (XII) (XIII)

Confirmation of the similarity of (XII) to chrysene was afforded by the resemblance in the absorption spectra of the two compounds (Fig. 1). The dissimilarity between the absorption spectrum of (IX) and the absorption spectra of (XI) and chrysene is an added proof of the *peri*-cyclization of (VIII) (Fig. 2).

Dr. Berenblum has examined (IX) and (XII) for their carcinogenic properties. Both the compounds were found to be inactive.

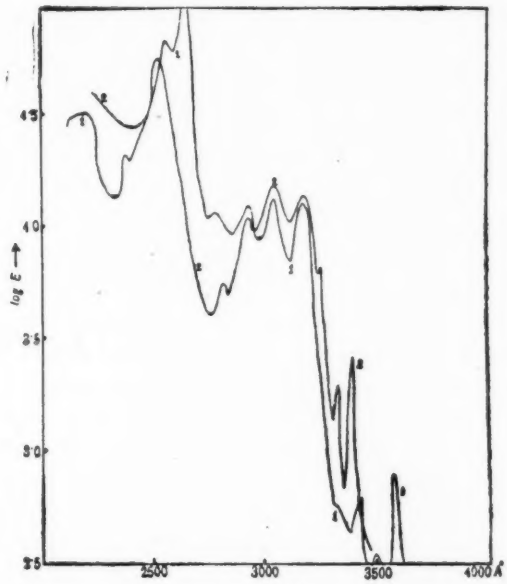


FIG. 1

(1) Chrysene (2) 4: 5, 5′: 4′—Dithionaphthene (XI).
Solvent—Methyl alcohol

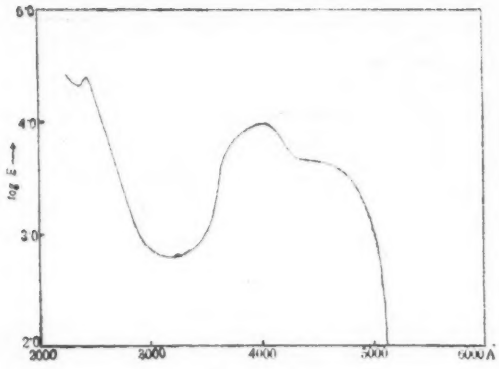


FIG. 2

1 : 6—Diathiapyrene (IX) Solvent—Methyl alcohol

EXPERIMENTAL

(Analyses are by Drs. Weiler and Strauss, Oxford. M.ps. are uncorrected.)

The cyclization of the liquid sulphides (I) and (III) was effected according to the general procedure outlined earlier.[1] They were characterized as the 2 : 4-dinitrophenylhydrazones of the parent *S*-naphthylthioglycolic-aldehydes. The sulphides (VIII) and (XI) also gave the corresponding *bis*-2 : 4-dinitrophenylhydrazones which, however, could not be purified.

β-Naphthyl ω-dimethoxyethyl sulphide (I).—β-Thionaphthol[7] (4·8 g.), sodium (0·7 g.), sodium iodide (0·45 g.), bromoacetaldehyde dimethyl acetal (5·1 g.), and absolute alcohol (70 c.c.) were boiled for 6 hours. The etherial solution of the reaction product after concentration, gave a brown solid which after crystallization gave lustrous colourless flakes, m.p. 138–39°, of di-β-naphthyl disulphide. The mother-liquor gave the sulphide as a colourless liquid, b.p. 158–60° (bath temp.)/0·1 mm. (2·82 g.). In spite of repeated distillations it could not be obtained in the analytically pure state. *2 : 4-Dinitrophenylhydrazone* gave small yellow-orange rods from benzene, m.p. 174° (Found: N, 14·4. $C_{18}H_{14}N_4O_4S$ requires N, 14·7%).

4 : 5-*Benzothionaphthene* (*II*).—The sulphide (I) (2·17 g.) was added to phosphorus pentoxide (15 g.) and phosphoric acid (9 c.c.) at 150°/0·1 mm. and the white solid obtained was dissolved in ether. After washing with water, the ether was removed when 4 : 5-benzothionaphthene was obtained, m.p. 114-15° (0·66 g.). Lustrous colourless flakes from light petroleum (60–80°), m.p. 116-17°. Mayer[2] gives m.p. 108–09° (Found: C, 78·6; H, 4·5. Calc. for $C_{12}H_8S$: C, 78·3; H, 4·4%). The phosphoric acid residue

after dilution with water, gave a further quantity of 4 : 5-benzothionaphthene which was isolated by ether and crystallized, m.p. 106–12° (0·22 g.). The *picrate* crystallized from alcohol in orange needles, m.p. 151° (Found: S, 8·1. $C_{18}H_{11}N_3O_7S$ requires S, 7·8%).

α-Naphthyl ω-dimethoxyethyl sulphide (*III*).—α-Thionaphthol[7] (9·8 g.), sodium (1·4 g.), sodium iodide (0·92 g.), bromoacetal (10·4 g.) and absolute alcohol (60 c.c.) were boiled for 2 hours. The reaction product (13·5 g.) after fractionation gave: (*a*) colourless liquid, b.p. 130–50° (bath temp.)/3 mm.; (*b*) pale yellow liquid, b.p. 170–80° (bath temp.)/3 mm. (10·3 g.). Fraction (*a*) was identical with di-α-naphthyl disulphide and fraction (*b*) after two redistillations gave the sulphide as a pale straw-coloured liquid, b.p. 175–80° (bath temp.)/2·5 mm. (Found: C, 68·0; H, 6·7. $C_{14}H_{16}O_2S$ requires C, 67·8; H, 6·5%). 2 : 4-*Dinitrophenylhydrazone* gave yellow microcrystalline powder from benzene, m.p. 184·5–85·5° (Found: N, 14·7. $C_{18}H_{14}N_4O_4S$ requires N, 14·7%).

Naphtho-(1′ : 8′-*bc*)-*thiapyran* (*IV*).—The sulphide (III) (2·46 g.) was added to a mixture of phosphorus pentoxide (15 g.) and phosphoric acid (9 c.c.) at 170–80°/2 mm. and the lemon-yellow liquid (0·97 g.) which distilled over was treated with alcoholic solution of picric acid (3·3 g.). The picrate was treated with 5% caustic soda solution and the mixture steam-distilled. Naphtho-(1′ : 8′-*bc*)-thiapyran was isolated by means of ether and distilled when it gave a greenish-yellow liquid, b.p. 150–55° (bath temp.)/1·5–2 mm. (Found: C, 78·2; H, 4·6. $C_{12}H_8S$ requires C, 78·3; H, 4·4%). The *picrate* crystallized in olive-brown needles from alcohol, m.p. 177–78° (Found: N, 10·6. $C_{18}H_{11}N_3O_8S$ requires N, 10·2%).

Naphthalene-1 : 5-*dithiol*.—An intimate mixture of naphthalene-1 : 5-disulphonic acid (40 g.) and phosphorus pentachloride (160 g.) was heated in an oil bath at 140–50° for 3 hours. Phosphorous oxychloride was removed by distillation under reduced pressure and the residue was added to crushed ice. The crude sulphonyl chloride gave colourless needles, m.p. 182–83° (22·0 g.) from benzene. The benzene mother-liquor on concentration, gave an impure crop of the sulphonyl chloride (5·6 g.).

The disulphonyl chloride was reduced to the dithiol in 85% yield by a modification of the method of Albenga and Corbellini[6] who obtained it in 50% yield. Absolute alcohol (230 c.c.) was saturated with dry hydrogen chloride at room temperature in a three-necked flask fitted with a reflux condenser and a calcium chloride tube. Hydrated stannous chloride (115 g.) was added and the solution brought to boil. The disulphonyl chloride (23 g.) in boiling benzene (250 c.c.) was gradually added. A vigorous reaction set in after each addition of the sulphonyl chloride. Dry hydrogen chloride was

passed through the reaction mixture throughout the experiment. The mixture was finally refluxed for 30 minutes and then distilled till 210 c.c. of the solvent distilled over. The residue gave lustrous pale yellow flakes of naphthalene-1 : 5-dithiol on cooling. The dithiol was collected on a sinter glass crucible, washed repeatedly with concentrated hydrochloric acid (total 115 c.c.), then with water and finally dried in vacuum over phosphorus pentoxide. The dithiol (11·5 g.) gave m.p. 118–20°. Albenga and Corbellini quote m.p. 119°.

1 : 5-Bis-*dimethoxyethylmercapto-naphthalene* (*VIII*).—Naphthalene-1 : 5-dithiol (5·76 g.), sodium (1·65 g.), sodium iodide (1 g.), bromoacetal (10·14 g.) and absolute alcohol (50 c.c.) were refluxed for 3 hours. After removal of alcohol, the residue was extracted with ether and the extract was concentrated when colourless flat needles of 1 : 5-*bis*-dimethoxyethylmercapto-naphthalene separated, m.p. 66–69° (4·46 g.), raised to 69–70° on further recrystallization from the same solvent (Found: C, 59·3; H, 6·5; S, 17·5. $C_{18}H_{24}O_4S_2$ requires C, 58·7; H, 6·5; S, 17·4%).

1 : 6-*Dithiapyrene* (*IX*).—Phosphoric acid (14·5 c.c.) was added to a mixture of phosphorus pentoxide (24 g.) and (VIII) (3 g.) and the mixture was immediately heated for 10 minutes in an oil-bath kept at 140–50°. The mixture was poured over crushed ice and the precipitate (2·1 g.) obtained was extracted repeatedly with boiling benzene. The benzene solution after decolourization and concentration (about 15 c.c.), gave lustrous orange needles of 1 : 6-dithiapyrene, m.p. 224–25° (65 mg.), unaltered by further recrystallizations. The mother-liquor gave 75 mg. of the crude material after removal of the solvent. A solution of the above product, m.p. 224–25°, in benzene gave a uniform chromatogram when passed through activated alumina indicating its homogeneity, and the product, thus purified, gave the same melting point as the product before chromatographic separation (Found: C, 70·1; H, 3·3; S, 26·6. M.W., 238. $C_{14}H_8S_2$ requires C, 70·0; H, 3·3; S, 26·7%; M.W., 240). *sym-Trinitrobenzene derivative* crystallized in lustrous black needles from benzene, m.p. 213–14° (Found: C, 53·5; H, 2·6. $C_{20}H_{21}N_3O_6S_2$ requires C, 53·0; H, 2·4%).

2 : 6-Bis-*dimethoxyethylmercapto-naphthalene* (*XI*).— Naphthalene-2 : 6-dithiol (4·05 g.), prepared as the 1 : 5-isomer, was boiled with sodium (1 g.), sodium iodide (0·3 g.), bromoacetal (7·13 g.), and absolute alcohol (50 c.c.) for 3 hours. The mixture was worked up as in (VIII). 2 : 6-*Bis*-dimethoxyethylmercapto-naphthalene gave colourless crystals from ether, m.p. 89–92° (3·23 g.), and a second crop of the product was also collected, m.p. 87–90° (1·0 g.). After recrystallization, colourless flakes were obtained, m.p. 92–93° (Found: C, 59·0; H, 6·5; S, 17·0. $C_{18}H_{24}O_4S_2$ requires C, 58·7; H, 6·5; S, 17·4%).

4:5, 5′:4′-*Dithionaphthene* (*XII*).—Phosphoric acid (14·5 c.c.) was added to phosphorus pentoxide (24 g.) and (XI) (3·0 g.), and the mixture immediately heated at 140–50° for 5 minutes and then worked up as in (IX). The reaction product (1·49 g.) was repeatedly extracted with hot benzene, and the benzene solution, after decolourization and concentration, gave pale yellow flat needles, m.p. 252–62° (0·42 g.). A solution of the latter in benzene was passed through a column of activated alumina, and the first fraction showing pale blue-violet fluorescence in ultra-violet light was collected. After concentration to about 15 c.c., the solution gave 4:5, 5′:4′-dithionaphthene as lustrous colourless flakes, m.p. 263–65° (0·31 g.), raised to 264–65° by further recrystallization (benzene) (Found: C, 70·2; H, 3·4; S, 26·2. $C_{14}H_8S_2$ requires C, 70·0; H, 3·3; S, 26·7%). The *sym-trinitrobenzene* derivative gave slender orange needles from benzene, m.p. 200–201° (Found: C, 53·0; H, 2·2. $C_{20}H_{11}N_3O_6S_2$ requires C, 53·0; H, 2·4).

Summary

4:5-Benzothionaphthene (II) was obtained by the α-cyclization of β-naphthyl ω-dimethoxyethyl sulphide (I), and the hitherto unknown naphtho-(1′:8′-*bc*)-thiapyran (IV) by the *peri*-cyclization of α-naphthyl ω-dimethoxyethyl sulphide (III).

Naphthalene-1:5-dithiol was obtained in 85% yield by an improved method. Condensation of naphthalene-1:5 and 2:6-dithiols with two molecules of bromoacetaldehyde dimethyl acetal gave (VIII) and (XI). The former cyclized in the *peri*-positions to give "1:6-thiapyrene" (IX) which was orange in colour, and the latter cyclized in the α-positions to give 4:5, 5′:4′-dithionaphthene (XII), an isoster of chrysene which was colourless. Chrysene and (XII) gave similar absorption spectra, which were markedly different from the absorption spectrum of (IX).

The author is indebted to Dr. I. Berenblum for testing the carcinogenic properties of (IX) and (XII).

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   Sunthankar and Tilak .. *Ibid.*, 396.
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A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part V. 6 : 7-Benzothionaphthene and 9-Chloronaphtho-(1′ : 8′-*bc*)-thiapyran

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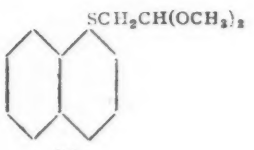
(*Department of Chemical Technology, University of Bombay*)

Received September 18, 1950

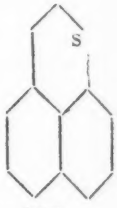
(Communicated by Dr. K. Venkataraman, F.A.SC.)

The product obtained by the cyclization of α-naphthyl ω-dimethoxyethyl sulphide (I), described in the previous communication, may be constituted either as 6 : 7-benzothionaphthene (II) or as naphtho-(1′ : 8′-*bc*)-thiapyran (III) depending on cyclization in the β- or the *peri*-positions. Unambiguous syntheses of (II) and (III) were therefore undertaken.



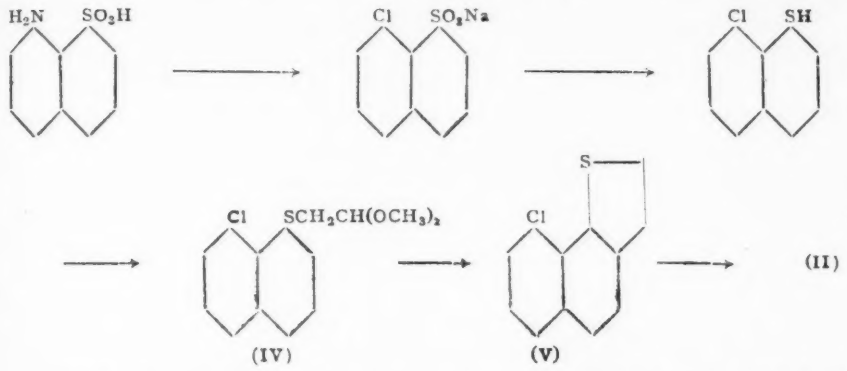
(I)

(II)



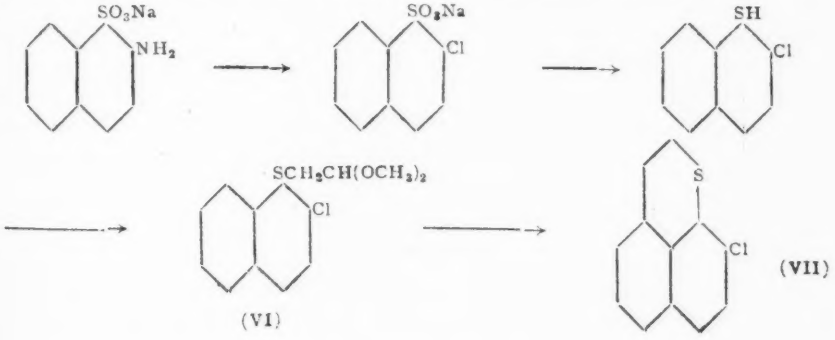
(III)

Sodium 8-chloronaphthalene-1-sulphonate, obtained in 80% yield by Sandmeyer reaction on 1-naphthylamine-8-sulphonic acid (*peri*-acid), was converted to 8-chloro-1-thionaphthol in 86% yield by the reduction of the intermediate 8-chloronaphthalene-1-sulphonyl chloride which was not isolated. Condensation of the thiol with bromoacetaldehyde dimethyl acetal gave 8-chloro-1-naphthyl ω-dimethoxyethyl sulphide (IV) in 70% yield and the latter on cyclization gave 3′-chlorobenzo-(1′ : 2′, 6 : 7)-thionaphthene (V) in 82% yield. Dechlorination of (V) yielded 6 : 7-benzothionaphthene (II), a pale straw-coloured liquid, b.p. 140–42° (bath temp.)/10 mm. (picrate : brick-red needles, m.p. 140–41°), which is different from the product, lemon-yellow liquid, b.p. 150–55° (bath temp.)/1·5–2 mm. (picrate : olive-brown needles, m.p. 177–78°), obtained by the ring-closure of (I) (*vide* previous communication). The latter product is therefore constituted as naphtho-(1′ : 8′-*bc*)-thiapyran (III).



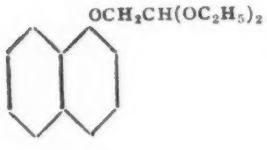
While the present work was in progress, Szmuszkovicz and Modest[1] have reported the synthesis of (II) by the Diels-Alder addition of maleic anhydride to 1-(2′-thienyl)-cyclohexene followed by dehydrogenation and decarboxylation of the adduct.

Synthesis of (III) starting from sodium 2-naphthylamine-1-sulphonate (salt of Tobias acid) was then undertaken. Sodium 2-chloronaphthalene-1-sulphonate was prepared by Sandmeyer reaction on Tobias acid. It is essential to treat the diazo salt from Tobias acid with cuprous chloride in concentrated hydrochloric acid to prevent the formation of 2-naphthol-1-sulphonic acid. 2-Chloro-1-thionaphthol was prepared from the sulphonic acid through the sulphonyl chloride, which was not isolated. The yield of the thiol starting from Tobias acid was 54%. Condensation of the thiol with bromoacetaldehyde dimethyl acetal, gave 2-chloro-1-naphthyl ω-dimethoxyethyl sulphide (VI) in good yield (71%), but due to the low yield (11%) of 9-chloronaphtho-(1′: 8′-*bc*)-thiapyran (VII) during cyclization of (VI), the dechlorination of (VII) to (III) could not be carried out.



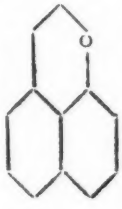
It is of interest to study the cyclization of α-substituted naphthalene derivatives. α-Naphthylacetic acid gives 9-keto-9:10-dihydroacenaphthene by *peri*-ring-closure.[2] Similarly β-1-naphthyl-propionic acids and γ-(5-methoxy-1-naphthyl)-butyric acid cyclize in the *peri*-positions.[3] Ingham *et al.*[4] cyclized α-naphthoxyacetyl chloride and obtained an isomer of 6:7-benzocoumaranone,[5] the properties of which suggested that it is probably the naphthopyrone obtained by *peri*-cyclization. Anand and Venkataraman[6] have, however, established the constitution of the cyclization product from α-naphthoxyacetic acid as 6:7-benzocoumaranone. Whereas the cyclization of β-thionaphthoxyacetic acid has been reported,[7] the ring-closure of α-thionaphthoxyacetic acid has not been recorded. 3-Hydroxynaphtho-(1′:8′-*bc*)-thiapyran and 3-hydroxy-6:7-benzothionaphthene which would result by the peri- or β-cyclization of α-thionaphthoxyacetic acid have been synthesized by Friedländer and Woroschzow[7] from *S*-8-carboxy-1-naphthyl thioglycolic acid and *S*-2-carboxy-1-naphthylthioglycolic acid respectively. Harley-Mason and Mann[8] experienced difficulty in the *peri*-cyclization of 2-chloro- and 2-acetamido-1-thionaphthoxyacetic acid. Whereas the *peri*-cyclization of α-thionaphthoxy derivatives is difficult and low yields of such cyclization products are to be expected, it is not impossible in view of the synthesis of (III) and (VII). Cyclization of α-thionaphthoxyacetic acid is of interest and is being studied.

Stoermer[9] has constituted the cyclization product of α-naphthoxyacetaldehyde diethyl acetal (VIII) as 6:7-benzocoumarone (IX), without adducing evidence of β-cyclization. The cyclization of α-naphthoxyacetic acid in the β-position,[6] supports the structure (IX) assigned by Stoermer. In view, however, of the *peri*-ring-closure of the sulphur analogue (I), the alternative naphthopyran structure (X) for the cyclization product cannot be ruled out. Unambiguous syntheses of (IX) and (X) have been undertaken.



(VIII)

(IX)



(X)

Experimental

The preparations of sodium 8-chloronaphthalene-1-sulphonate and sodium 2-chloronaphthalene-1-sulphonate from the corresponding amino

sulphonic acids have been described as convenient laboratory methods for the preparation of these acids are not available. Similarly, the syntheses of 8-chloro-1-thionaphthol and 2-chloro-1-thionaphthol from the above acids are also described.

The condensation of the chlorothionaphthols with bromoacetaldehyde dimethyl acetal and the isolation of the sulphides (IV) and (VI) were carried out according to the general procedure outlined earlier.[10] The sulphides being viscous oils, were dissolved in dry benzene and the benzene solution was added to a hot mixture of phosphorus pentoxide and phosphoric acid under the general conditions described earlier.[10]

The sulphides (*S*-arylthioglycolic-aldehyde dimethyl acetals) were characterized by the preparation of 2:4-dinitrophenylhydrazones of the parent *S*-arylthioglycolic-aldehydes, and the cyclized products were characterized as picrates.

Sodium 8-chloronaphthalene-1-sulphonate.—Commercial *peri*-acid (28 g.; 85% purity) was extracted with a hot suspension of magnesium oxide (3 g.) in water (175 c.c.) at 95° C. and the solution of the magnesium salt of the acid, after cooling to room temperature (25°) by addition of ice, was treated with 30% sulphuric acid (75 g.) under stirring. The finely divided suspension of the acid was diazotized at room temperature by addition of an aqueous solution of sodium nitrite (10 g. in 25 c.c.). The nitrite solution was added gradually in two hours below the surface of the liquid. After leaving overnight under stirring, the diazo salt which precipitated was filtered and washed with a little ice-cold water, made into a slurry with water and then added gradually to freshly prepared cuprous chloride [from copper sulphate (19·0 g.), sodium chloride (11·2 g.) and sodium sulphite (11·2 g.)] and concentrated hydrochloric acid (8 c.c.) at 30–35°. After the completion of the reaction (no colour with an alkaline solution of R-salt), the mixture was warmed to 55° and the precipitated naphthasultone was filtered. The filtrate was made alkaline and the precipitated copper salts filtered using 'supercel' filter-aid. Sodium 8-chloronaphthalene-1-sulphonate was salted out by adding 25 g. of salt per 100 c.c. of the solution, collected and washed with saturated brine and dried (26 g. of 95% pure sodium salt; yield 87%). Concentration of the mother liquor gave a second crop of the impure salt.

8-*Chloro*-1-*thionaphthol.*—A mixture of sodium 8-chloronaphthalene-1-sulphonate (15 g.), phosphorus pentachloride (16 g.) and dry chloro benzene (127 g.) was heated at 78–80° under stirring till the evolution of hydrogen chloride ceased. After cooling to 10°, 30% sulphuric acid (110 g.) was added followed by zinc dust (23 g.), keeping the temperature below 30°,

The mixture was raised to 70° in 30 minutes and maintained at this temperature for one hour. Chlorobenzene was steam distilled, the residue cooled and poured into ice. The crude thiol was filtered, extracted with peroxide-free ether, and the thiol (9·0 g., yield 86%), m.p. 106–108°, recovered by removal of the solvent.

8-*Chloro*-1-*naphthyl ω-dimethoxyethyl sulphide* (*IV*).—The above thiol (8·75 g.), sodium (1·1 g.), bromoacetal (9 g.) and absolute alcohol (50 c.c.) were refluxed for 6 hours. The crude sulphide (8·9 g.; yield 70%) on repeated distillation gave a viscous brown oil, b.p. 164–66° (bath temp.)/6 mm., which however did not give correct elementary analysis. The sulphide gave 2:4-*dinitrophenylhydrazone* of the parent *S*-(8-chloro-1-naphthyl)-thiolglycolic-aldehyde. The hydrazone crystallized from ethyl acetate in yellow needles, m.p. 179·5° (Found: C, 51·4; H, 3·0; Cl, 7·8, N, 13·4. $C_{18}H_{13}ClN_4O_4S$ requires C, 51·8; H, 3·1; Cl, 8·5; N, 13·4%).

3′-*Chlorobenzo*-(1′:2′, 6:7)-*thionaphthene* (*V*).—A solution of the sulphide (IV) (5 g.) in benzene (20 c.c.) was added gradually to a mixture of phosphorus pentoxide (25 g.) and phosphoric acid (15 c.c.) at 200°/8–10 mm. A small amount of cyclized product distilled over, but the major portion was recovered by ether extraction of the phosphoric acid mixture after dilution with water. The combined product (4·23 g.), m.p. 76–78°, was treated with a saturated solution of picric acid (5 g.) and the picrate was decomposed with 1% ammonia, and the thionaphthene was recovered by extraction with ether. Evaporation of the solvent, gave the purified thionaphthene (3·2 g.; yield 82%), m.p. 81–82°, raised to 83° by recrystallization from aqueous alcohol, when it gave pale straw-coloured needles (Found: C, 65·7; H, 3·3. $C_{12}H_7ClS$ requires C, 65·8; H, 3·2%). The *picrate* gave orange-yellow needles from alcohol, m.p. 160° (Found: N, 9·4. $C_{15}H_{10}ClN_3O_7S$ requires N, 9·4%).

6:7-*Benzothionaphthene* (*II*).—The above chlorobenzothionaphthene (0·65 g.), magnesium turnings (1·3 g.), a drop of methyl iodide and absolute methyl alcohol (50 c.c.) were refluxed for ten hours, when most of magnesium reacted. After distillation of alcohol, the residue was acidified with 5% hydrochloric acid (200 c.c.) and the mixture extracted three times with ether (30 c.c. each time). The combined ether extract after drying (sodium sulphate) and removal of solvent gave an oil (0·52 g.) which on fractional distillation in a bulb-tube gave 6:7-benzothionaphthene (II), light straw-coloured liquid (0·24 g.), b.p. 140–45° (bath temp.)/10 mm. and unreacted (V), pale yellow solid (0·25 g.), m.p. 75–77°, b.p. 155–60° (bath temp.)/10 mm. The yield of (II) taking into account the recovered (V) is 71%. Redistillation

of crude (II) gave light straw-coloured liquid, b.p. 140–42° (bath temp.)/10 mm. (Found: C, 78·8; H, 4·7. $C_{12}H_8S$ requires C, 78·3; H, 4·3%). The *picrate* gave orange-red needles from alcohol, m.p. 140·5–41·5° (Found: C, 51·8; H, 2·7; N, 10·8. $C_{18}H_{11}N_3O_7S$ requires C, 52·3; H, 2·7; N, 10·2%).

Sodium 2-chloronaphthalene-1-sulphonate.—An aqueous solution of sodium salt of Tobias acid (43·5 g. in 150 c.c.) was decolourized (Norit), acidified with acetic acid (30 c.c.) and 50% sulphuric acid (100 c.c.), the mixture cooled to 5° and an aqueous solution of sodium nitrite (15 g. in 25 c.c.) was gradually added under stirring. The mixture was diazotized for one hour below 10° and the insoluble diazo salt was filtered, washed with a little ice-cold water and gradually added to a solution of freshly prepared cuprous chloride (from 40 g. copper sulphate) in hydrochloric acid (100 c.c.), keeping the temperature below 15°. After working for one hour, the mixture was warmed to 55° and filtered. The filtrate was made alkaline to precipitate copper salts, and the mixture filtered through a bed of supercel filter-aid. The filtrate was concentrated to half the bulk, cooled, and the crude sodium 2-chloronaphthalene-1-sulphonate collected and dried in vacuum at 60° (yield 40 g., the crude salt contains some sodium chloride). Evaporation of the mother liquor gave a further crop of the impure product.

2-Chloro-1-thionaphthol.—The thiol was prepared as in the case of 8-chloro-1-thionaphthol starting from crude sodium 2-chloronaphthalene-1-sulphonate (20 g.), phosphorus pentachloride (21·5 g.) and chlorobenzene (36 g.). The crude thiol (8 g., yield 54% on the basis of the Tobias salt) was crystallized three times from aqueous alcohol, when it gave pale yellow crystals, m.p. 65·5°. Dosser and Richter[11] give m.p. 66·5° (Found: C, 61·2; H, 3·7. $C_{10}H_7ClS$ requires C, 61·7, H, 3·6%). Oxidation of the thiol with alcoholic ferric chloride, gave the disulphide which crystallized from *n*-hexane in pale yellow diamond-shaped crystals, m.p. 138°. Dosser and Richter[11] give m.p. 134° (Found: C, 61·4; H, 2·9. $C_{20}H_{12}Cl_2S_2$ requires C, 62·0; H, 3·1%). Condensation of the thiol with chloroacetic acid in alkaline solution gave the corresponding thioglycolic acid, which crystallized from water in colourless needles, m.p. 98·5°. Harley-Mason and Mann[12] give, m.p. 95–97° (Found: C, 57·0; H, 3·5. $C_{12}H_9ClO_2S$ requires C, 57·0; H, 3·6%).

2-Chloro-1-naphthyl ω-dimethoxyethyl sulphide (*VI*).—2-Chloro-1-thionaphthol (9 g.) was condensed with bromoacetal (9 g.) as in the preparation of (IV). The crude sulphide (9·35 g., yield 71·5%) after four distillations gave a colourless oil, b.p. 163–68° (bath temp.)/5–6 mm. (Found: C, 60·1; H, 6·1. $C_{14}H_{15}ClO_2S$ requires C, 59·5; H, 5·3%). *2:4-Dinitrophenyl-*

hydrazone crystallized in yellow needles from *n*-hexyl alcohol, m.p. 165° (Found: N, 13·5. $C_{18}H_{13}ClN_4O_4S$ requires N, 13·4%).

9-*Chloronaphtho*-(1′: 8′-*bc*)-*thiapyran* (*VII*).—The sulphide (VI) (5 g.) was cyclized with a mixture of phosphorus pentoxide (25 g.) and phosphoric acid (15 c.c.) as in the preparation of (V). The crude thiapyran (0·43 g., yield 11%) was crystallized from *n*-hexane, then distilled at 190–200° (bath temp.)/11 mm. and finally purified by crystallization from *n*-hexane, when it gave stout yellow needles, m.p. 121° (Found: C, 65·4; H, 3·5. $C_{12}H_7ClS$ requires C, 65·8; H, 3·2%). The *picrate* crystallized from alcohol in greenish black needles, m.p. 169°.

Summary

8-Chloro-1-thionaphthol, prepared from *peri*-acid, was condensed with bromoacetaldehyde dimethyl acetal to give 8-chloro-1-naphthyl ω-dimethoxyethyl sulphide (IV). Ring-closure of (IV) gave 3′-chlorobenzo-(1′: 2′, 6: 7)-thionaphthene (V), which on dechlorination gave 6: 7-benzothionaphthene (II). The cyclization product from α-naphthyl ω-dimethoxyethyl sulphide (I) reported in the previous communication being different from (II) is therefore naphtho-(1′: 8′-*bc*)-thiapyran (III).

9-Chloronaphtho-(1′: 8′-*bc*)-thiapyran (VII) was prepared from Tobias acid in a manner similar to (V), but dechlorination of (VII) to (III) could not be carried out due to the low yields of (VII) in the cyclization of 2-chloro-1-naphthyl ω-dimethoxyethyl sulphide (VI).

The literature on the cyclization of certain related α-substituted naphthyl, naphthoxy and thionaphthoxy derivatives is discussed.

The authors are indebted to Mr. T. S. Gore for the microanalyses recorded in the paper.

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A NEW SYNTHESIS OF THIOPHENES AND THIAPYRANS

Part VI. 7 : 8-Benzothiophanthrene

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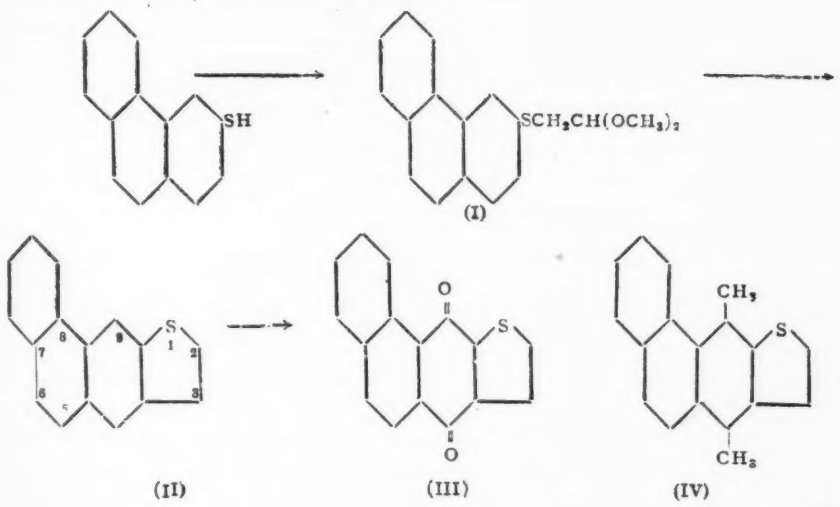
Received September 18, 1950

(Communicated by Dr. K. Venkataraman, F.A.SC.)

THE syntheses of a series of benzothiophenes, naphthothiophenes and naphthothiapyrans starting from thiophenols and naphthalene thiols have been described in the previous communications.[1] Among the thiophenophenanthrenes only thiopheno-3, 4 : 9′, 10′-phenanthrene[2] and thiopheno-2, 3 : 3′, 4′-phenanthrene[3] have been reported.

To extend the application of the new synthesis of thiophenes and thiapyrans to thiophenophenanthrenes and also with a view to prepare 4 : 9-dimethyl-7 : 8-benzothiophanthrene (IV), the sulphur-isoster of the highly carcinogenic hydrocarbon 9 : 10-dimethyl-1 : 2-benzanthracene, phenanthrene-3-thiol was converted to 7 : 8-benzo-4 : 9-thiophanthrenequinone (III), the precursor to (IV) by the following scheme:



Condensation of phenanthrene-3-thiol with bromoacetaldehyde dimethyl acetal gave 3-phenanthryl ω-dimethoxyethyl sulphide (I) as a transparent colourless glassy jelly. Cyclization of (I) gave 7:8-benzothiophenanthrene (II) which after exhaustive purification gave lustrous colourless flakes, m.p. 81–82°. In γ-3-phenanthrylbutyric acid or in substituted acids with substituents in the nucleus or in the side chain, 3:2-cyclization leading to 1:2-benzanthracene derivatives is generally observed.[4] The ring-closure of (I) should therefore lead to (II) by 3:2-cyclization, a conclusion which was confirmed by oxidation to the quinone which appears to be identical with the quinone (III) prepared by Sandin and Kitchen[5] starting from thiophene and naphthalene-1:2-dicarboxylic anhydride. The synthesis of the dimethyl compound (IV) from the quinone (III) was discontinued in view of the same preparation carried out by the above authors.

Dr. Berenblum has examined the carcinogenic activity of 7:8-benzothiophanthrene and found it to be inactive.

Experimental

(Analyses are by Drs. Weiler and Strauss, Oxford. M.p.s. are uncorrected.)

3-Phenanthryl ω-dimethoxyethyl sulphide (I)

Phenanthrene-3-sulphonyl chloride[6] was reduced to phenanthrene-3-thiol[7] and the latter (3·15 g.) was boiled with sodium (0·35 g.), sodium iodide (0·23 g.), bromoacetal (2·54 g.) and absolute alcohol (60 c.c.) for 3 hours. The sulphide gave a transparent viscous jelley after three distillations, b.p. 190–200° (bath temp.)/0·12 mm. (Found: S, 10·7. $C_{18}H_{18}O_2S$ requires S, 10·7%). 2:4-*Dinitrophenylhydrazone* of *S*-(3-phenanthryl)-thioglycolic-aldehyde gave short orange needles from benzene, m.p. 193–94° (Found: C, 61·3; H, 3·9; N, 12·8. $C_{22}H_{16}N_4O_4S$ requires C, 61·1; H, 3·7, N, 13·0%).

7:8-Benzothiophanthrene (II)

Phosphoric acid (6 c.c.) was added to a mixture of the sulphide (I) (1·78 g.) and phosphorus pentoxide (10 g.), and the mixture was immediately heated in an oil-bath kept at 135–45° for 3 minutes and then diluted with crushed ice. The product was isolated by extraction with ether, dissolved in benzene and the solution was passed through a column of activated alumina using ether for developing the chromatogram. The fraction giving violet-blue fluorescence in ultra-violet light was collected, and after evaporation of the solvent, the product (0·97 g.) was treated with alcoholic solution of picric acid (2 g.). The product, m.p. 75–77°, obtained

by decomposition of the picrate, was distilled when a cream-coloured solid (0·5 g.) b.p. 190–200° (bath temp.)/0·012 mm. was obtained. A solution of this product in ether-alcohol, after partial removal of ether under reduced pressure, gave 7:8-benzothiophanthrene as lustrous colourless flakes, m.p. 81–82° (Found: C, 82·0; H, 4·4; S, 13·5. $C_{16}H_{10}S$ requires C, 82·1; H, 4·3; S, 13·7%). The *picrate* gave short orange needles from absolute alcohol, m.p. 154–55° (Found: N, 8·7. $C_{22}H_{13}N_3O_7S$ requires N, 9·1%).

7:8-*Benzo*-4:9-*thiophanthrenequinone* (*III*)

A solution of chromium trioxide (1 g.) in acetic acid (2·5 c.c.) and water (2·5 c.c.) was added to a boiling solution of 7:8-benzothiophanthrene (0·5 g.) in acetic acid (20 c.c.) and the resulting solution was boiled under reflux for 15 minutes. After dilution in water, the mixture was extracted with benzene and the extract after washing and drying (Na_2SO_4) was concentrated and passed through a column of activated alumina. The pale yellow fraction, after concentration to about 1 c.c. and addition of a few drops of light petroleum (60–80°) gave orange needles of the quinone, m.p. 204–05°, unaltered by further recrystallization. Sandin and Kitchen[5] give, m.p. 202–04° (Found: C, 73·1; H, 3·4. Calc. for $C_{16}H_8O_2S$: C, 72·7; H, 3·0%).

Summary

Condensation of phenanthrene-3-thiol with bromoacetaldehyde dimethylacetal gave 3-phenanthryl ω-dimethoxyethyl sulphide (I) which on cyclization gave 7:8-benzothiophanthrene (II). The latter on oxidation gave 7:8-benzo-4:9-thiophanthrenequinone (III) identical with the quinone obtained by Sandin and Kitchen[5] by a different method.

The author is deeply grateful to Dr. I. Berenblum for examining the carcinogenic potency of (II).

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NENCKI'S REACTION WITH CRESOLS

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Received March 14, 1950

Nencki's reaction which involves the condensation of an organic acid and a phenol in the presence of anhydrous zinc chloride[1] does not appear to have been studied in any detail with reference to cresols. Of the three cresols only with *m*-cresol the reaction was tried using propionic and butyric acids, and 4-acyl derivatives were produced.[2]

The condensation of *o*- and *p*-cresols with acetic, propionic and butyric acids has now been studied according to the conditions of Nencki's reaction. So also the interaction between *m*-cresol and acetic acid has been tried to complete the series. In the latter case 4-acetyl-*m*-cresol has been obtained. With *o*-cresol both *o*- and *p*- substituted derivatives have been produced in different proportions, while with *p*-cresol only the 5-acyl derivative is the product. In all the cases the yields vary with the duration of heating and each reaction has its optimum period for the maximum yield.

It may be noted that in the above condensations the yields produced are lower than those obtained by the isomerization of the corresponding phenol esters according to Fries reaction.

Experimental

m-Cresol was condensed with acetic acid and *o*- and *p*-cresols with acetic, propionic and butyric acids according to the following general procedure:—The cresol (10 g.) was added to the appropriate acid (10 c.c.) in which anhydrous zinc chloride (10 g.) had been dissolved previously by heating. The mixture was then heated under reflux for different periods of time. After the heating was over, it was cooled, treated with 100 c.c. of 50 per cent. hydrochloric acid and left overnight. On extraction with ether an oily product mixed with some resin was obtained. When this mixture was subjected to steam distillation, a part passed over along with steam, while the rest remained in the distillation flask. The volatile portion consisted of a mixture of some unreacted original phenol and a ketone, and their separation was effected by taking advantage of the fact that when the mixture was dissolved in hot 5 N sodium hydroxide and cooled, the ketone separated as the sodium salt in pale-yellow crystals. The latter on decompo-

sition with dilute hydrochloric acid regenerated the ketone, which could be purified by distillation under reduced pressure.

The nonvolatile residue remaining after the steam distillation contained another isomeric ketone in some cases. Wherever it was formed, it was isolated by extraction with ether and purified by crystallization from either hot water or dilute alcohol.

It may be noted that the steam-volatile ketones contained the ketonic group in *ortho* position to the hydroxyl and produced the characteristic colours on treatment with ferric chloride. They are mostly liquids at the ordinary temperature.

Condensation of m-*cresol with acetic acid*

Only the steam-volatile ketone was produced in this case. It boiled at 126°/20 mm. and at 245° at atmospheric pressure. It was identified as 2-hydroxy-4-methylacetophenone, since it formed the semicarbazone and the oxime melting at 214° and 132° respectively. The variation of the yields of the ketone with the duration of heating is given below:—

TABLE I

Sl. No.	Duration of heating	Yield of 4-acetyl-m-cresol (2-hydroxy-4-methylacetophenone)
1	5 minutes	Nil
2	1 hour	15%
3	3 hours	20%
4	4 ,,	22%
5	6 ,,	25%
6	7 ,,	Much resinification

Condensation of o-*cresol*

(*a*) *With acetic acid.*—Two ketones, *viz.*, 2-hydroxy-3-methylacetophenone (b.p. 106°–07°/10 mm.; semicarbazone, m.p. 228°; phenyl hydrazone, m.p. 122°) and 4-hydroxy-3-methylacetophenone (m.p. 104°; oxime, m.p. 93°–94°)[3] were obtained.

(*b*) *With propionic acid.*—2-Hydroxy-3-methylpropiophenone (b.p. 127°–29°/15 mm.; semicarbazone, m.p. 202°) and 4-hydroxy-3-methylpropiophenone (m.p. 83°–84°; 2:4-dinitrophenyl hydrazone, m.p. 238°[4]) were obtained.

(*c*) *With butyric acid.*—2-Hydroxy-3-methylbutyrophenone (b.p. 142°–43°/10 mm.; oxime, m.p. 87°–88°; phenyl hydrazone, m.p. 157°–58°) and 4-hydroxy-3-methylbutyrophenone (m.p. 132°–33°; phenyl hydrazone, m.p. 110°) were formed. Some difficulty was experienced in the preparation of the oxime and phenyl hydrazone derivatives of the 2-hydroxy-3-methylbutyrophenone. However, the ketone reacted with 2:4-dinitrophenylhydrazine very readily to produce the 2:4-dinitrophenylhydrazone. For the condensation, it (1 g.) was treated with dinitrophenylhydrazine (1 g.) dissolved in concentrated sulphuric acid (2 c.c.) and refluxed after the addition of 15 c.c. of alcohol on a water-bath for half an hour. The derivative crystallized out from acetic acid as brick-red, narrow rectangular plates, and melted at 190°–92° (Found: C, 56·36; H, 4·81; $C_{17}H_{18}O_5N_4$ requires C, 56·98; H, 5·03%).

In all the above condensations the yields varied with the duration of heating and the results are given below:—

TABLE II

Duration of heating	With acetic acid		With propionic acid		With butyric acid	
	2-Hydroxy-3-methylacetophenone	4-Hydroxy-3-methylacetophenone	2-Hydroxy-3-methylpropiophenone	4-Hydroxy-3-methylpropiophenone	2-Hydroxy-3-methylbutyrophenone	4-Hydroxy-3-methylbutyrophenone
5 minutes ..	5%	10%	4%	11%	Nil	8%
15 ,, ..	..	..	12·5%	8·5%	..	..
30 ,, ..	..	..	25%	6%	..	..
1 hour ..	15%	8%	21%	3%	5%	10·5%
1·5 hours ..	..	..	14%	2%	..	..
2 ,, ..	20%	5%	..	..	8%	4·5%
4 ,, ..	..	..	..	..	4%	2%

Condensation of p-*cresol with acetic, propionic and butyric acids*

p-Cresol underwent condensation with acetic, propionic and butyric acids yielding respectively 6-hydroxy-3-methylacetophenone (m.p. 50°; oxime, m.p. 145°; semicarbazone, m.p. 211°–12°), 6-hydroxy-3-methylpropiophenone (b.p. 153°/40 mm.; phenylhydrazone, m.p. 146°; oxime, m.p. 134°–35°) and 6-hydroxy-3-methylbutyrophenone (b.p. 132°/15 mm.; oxime, 96°–97°; semicarbazone, m.p. 188–89°). The yields of the different ketones obtained when the reaction mixtures were heated for different times are recorded below:—

TABLE III

Duration of heating	With acetic acid	With propionic acid	With butyric acid
	6-Hydroxy-3-methyl acetophenone	6-Hydroxy-3-methyl propiophenone	6-Hydroxy-3-methyl butyrophenone
5 minutes ..	2%	..	..
15 ,, ..	..	27%	15%
1 hour ..	10%	55%	24%
2 hours ..	14%	50%	27%
3 ,, ..	12%	..	..
4 ,, ..	Much resinification	35%	24%
5 ,, ..	..	..	18%

SUMMARY

The condensation of cresols with acetic, propionic and butyric acids was tried under conditions of Nencki's reaction employing anhydrous zinc chloride as the condensing agent. Only *o*-cresol gave rise to both the *ortho*- and *para*-substituted derivatives, while the *m*- and the *p*-cresols produced only the *ortho*-substituted products. The yields varied with the duration of heating.

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A NEW ADSORPTION ISOTHERM

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Received August 14, 1950

The phenomenon of adsorption has been engaging the attention of a large number of workers on account of its theoretical interest as well as its extensive application in the studies of colloidal behaviour and life processes of cells, etc. and above all in industrial reactions. It deals with the retention of molecules from gases or solutions at the surface of adsorbents, which are usually solids. It has been found convenient to differentiate between "physical adsorption" and "chemisorption". In the former the surface forces involved are of the Van der Waals type and are not so specific in character and the strength of binding is moderate, while in "chemisorption" the surface forces are similar to those active in chemical reactions and are specific in nature and the binding is stronger and corresponds to that found in chemical processes.

Several mathematical equations have been given, of which the more important are stated below:—

(*a*) Gibb's equation, *viz.*, $a = -\frac{c}{\mathrm{K}1} \cdot \frac{d\sigma}{dc}$ has been derived thermodynamically and relates "a" the amount adsorbed at the interface to the concentration C, temperature T and the variation of the surface tension with concentration. Although the earlier experiments of McBain and Davies[1] revealed discrepancies from this equation, the more recent work of McBain and his co-workers[2] appears to give quantitative agreement with Gibb's expression.

(*b*) Freundlich's isotherm, $a = k \cdot c^{\frac{1}{n}}$, is empirical and relates the amount adsorbed a to the concentration C, (K and n being constants). This has been found to be in agreement with some of the experimental data, but does not give any clear picture of the mechanism of adsorption.

(*c*) An important theoretical treatment based on kinetic considerations has led Langmuir to propose the following equation:

$$a = \frac{a\mu c}{1 + \mu c}.$$

Volmer derived an equation of the same form from thermodynamic considerations. In contrast to the Freundlich's equation, which cannot describe the adsorption of gases completely from the lowest to the highest pressure region, Langmuir's equation is capable of fitting experimental data more adequately.[3] The Freundlich equation however fits most cases of adsorption from solutions better than the Langmuir equation.

(*d*) An account of the adsorption isotherms proposed by other workers can be found in standard books[4] on this subject. Of these one of the most important equations was that derived by Brunauer, Emmet and Teller[5] on the basis of a theory of multimolecular adsorption, namely,

$$\frac{v}{v_m} = \frac{cp}{(p_0 - p)\left\{1 + (c-1)\frac{p}{p_0}\right\}},$$

where C is a constant, V_m—(a constant)—the volume of the gas required to form a complete unimolecular layer on the adsorbent, p_0 the saturation pressure of the gas, and V the volume of the gas adsorbed at a pressure p. If only a limited number of layers are adsorbed, they obtained the equation:

$$\frac{v}{v_m} = \frac{cx}{1-x} \cdot \frac{1 - (n+1)x^n + nx^{n+1}}{1 + (c-1)x - cx^{n+1}},$$

where $x = \frac{p}{p_0}$ and n is the maximum number of layers. Where only one adsorbed layer is formed on the surface of the adsorbent the above equation reduces to one of the Langmuir type, *viz.*,

$$\frac{v}{v_m} = \frac{\frac{c}{p_0} \cdot p}{1 + \frac{c}{p_0} \cdot p}$$

The B. E. T. equations referred to above fit in three types of isotherms, one of which is an S-shaped curve, which is concave to the pressure axis at low pressures and convex at higher pressures. In order to make their theory applicable to other types of adsorption curves, S. Brunauer, L. S. Deming, W. E. Deming and E. Teller[6] obtained a more general equation, *viz.*,

$$\frac{v}{v_m} = \frac{cx}{1-x} \cdot \frac{1 + (\frac{1}{2}ng - n)x^{n-1} - (ng - n + 1)x^n + \frac{1}{2}ngx^{n+1}}{1 + (c-1)x + (\frac{1}{2}cg - c)x^n - \frac{1}{2}cgx^{n+1}},$$

where $g = e^{Q/RT}$, and the other terms have the same meaning as that indicated above.

A. B. D. Cassie[7] using a general statistical method has shown that the equation deduced for the adsorption isotherm with localised sites is identical

with the B. E. T. equation, and that this equation is only applicable to systems where adsorption occurs as distinct clusters of molecules and not to multimolecular adsorption as continuous layers superposed on a continuous monolayer. In a paper dealing with the examination of the theory of Brunauer and Coworkers, S. J. Gregg and Jacobs[8] have pointed out the merits and deficiencies of this theory. The B. E. T. equation has also been modified by Anderson.[9]

The application of Brunauer's equations to different types of adsorption curves has been discussed in Brunauer's "Physical Adsorption of gases and vapours (1943, pages 155 to 177)." Some difficulty was experienced in the proper interpretation of S-shaped curves—like those obtained by Coolidge in regard to the adsorption of water vapour on charcoal—which are convex to the pressure axis at low pressures and concave at high pressures. A new adsorption equation derived by the author is presented in this paper, which, although primarily derived to explain such S-shaped curves, can also be applied to some other types of adsorption processes.

Derivation

When the molecules (say in a gas or solution) impinge on the surface of an adsorbent, some of them are retained on the surface by virtue of the surface forces for a certain length of time depending upon the strength of the force, to form the first layer of adsorbed molecules. When more molecules strike this surface, they may be retained if the intermolecular forces of the adsorbate are strong enough to overcome the tendency of these outer molecules to escape into the gas or solution phase again. (This will lead to the formation of a second and even higher adsorbed layers.) We then obtain a condition, where the previously adsorbed molecules facilitate the adsorption of more molecules striking them. Under such conditions, which are quite likely to occur, the rate of increase of adsorption with increase in the concentration of the molecules in the space above the adsorbent will depend upon the number of molecules already adsorbed and also upon the concentration of the molecules still available for adsorption in the free state in the gas or solution. This can be expressed mathematically as follows:—

$$\frac{dn}{dc} = k \cdot n\,(\mathrm{A} - n), \tag{1}$$

where n is the number of molecules adsorbed, and A is the total number of molecules originally present in the gas space or solution. On integration and rearrangement this can be transformed into the following equation:—

$$n = \frac{\mathrm{A}}{1 + \alpha \cdot e^{-\mathrm{K}c}} \tag{2}$$

n—the number of molecules adsorbed (say per unit mass of adsorbent), c is the concentration of the free molecules in the gas space above, and α and K are constants.

If the rate of increase of the number of the adsorbed molecules is also dependent upon factors which vary with the number of the molecules already adsorbed, then the more generalized equation can be written as follows:

$$\frac{dn}{dc} = k \cdot n\,(\mathrm{A} - n) \cdot f(c) \tag{3}$$

which on integration and rearrangement gives

$$\frac{\mathrm{A} - n}{n} = \alpha \cdot e^{-\mathrm{KA} \int f(c) \cdot dc}$$

or,

$$n = \frac{\mathrm{A}}{1 + \alpha \cdot e^{-\mathrm{KA} \int f(c) \cdot dc}} \text{ or } \frac{\mathrm{A}}{1 + \alpha \cdot e^{\mathrm{F}(c)}} \tag{4}$$

The function $\mathrm{F}(c)$ may be expressed in a form which will enable us to fit in the experimental data. If $\mathrm{F}(c) = -kc$ we get equation (2). If $\mathrm{F}(c)$ is represented by a series such as $k_1c + k_2c^2 + k_3c^3 \ldots$, then

$$n = \frac{\mathrm{A}}{1 + \alpha \cdot e^{k_1c + k_2c^2 + k_3c^3 \cdot}} \tag{5}$$

Such an equation will be helpful in fitting in curves showing maxima and minima such as those obtained in the sorption of colloids. Adsorption curves are of different shapes and by assigning to $\mathrm{F}(c)$ a suitable value it may be possible to fit in such curves.

Equation (2) can also be written in the following form:

$$n = \frac{\mathrm{A} \cdot c^{kc}}{\alpha + e^{kc}}$$

whereas Langmuir's equation may be expressed as

$$n = \frac{\mathrm{A} \cdot kc}{\alpha + kc}.$$

At low concentrations equation (2) reduces to $n = \beta \cdot e^{kc}$ or $\beta(1 + kc)$. Actually at low concentrations the isotherms are found to be linear while at high concentrations n becomes approximately equal to a constant—a result borne out by actual observations.

The wide range of applicability of the equation (2) derived in the previous section is evident from the fact that in a number of adsorption processes typical S-shaped curves are obtained, which should fit in very well

with this equation. As an example one could consider the curves obtained by Coolidge[10] and McBain and Co-workers[11] relating to the adsorption of water vapour on charcoal. Even in quite a different field of investigation involving the adsorption of bacteria by well-known adsorbents like charcoal and kaolin the equation derived by the author has found application. It will be of interest to examine more data on adsorption with a view to test the validity of this equation.

Summary

A new adsorption equation, *viz.*, $a = \frac{A}{1 + \alpha \cdot e^{-kc}}$ has been derived for those cases of adsorption where the previously adsorbed molecules facilitate the adsorption of more molecules striking the surface of the adsorbent. This equation fits in well with the adsorption data yielding the familiar S-shaped curves and should find extensive application.

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PHOTOMETRY OF RAMAN SPECTRA OF CRYSTALS—PART II

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Received December 20, 1950

(Communicated by Prof. R. S. Krishnan, F.A.SC.)

1. Introduction

In earlier communication which appeared in these *Proceedings* (and which will be referred to as Part I) the author (Narayanan, 1948) outlined a new method of determining accurately the relative intensity of Raman lines and also the ratio of intensity of the Stokes and anti-Stokes components of a Raman line by the use of an ultraviolet Spekker photometer. However, as the instrument then available was not in perfect order, it was not possible to use it for accurate measurements in the case of high frequency Raman lines. Recently, the work was resumed with a new Spekker photometer. Using this instrument, Krishnan and Narayanan (1950) measured the relative intensities of the Raman lines in diamond.

2. Experimental Results and Discussion

For an accurate determination of the relative intensities by photographic photometry, it is well known that the only correct method is to attempt to produce the two images to be of equal density on the same plate and with the same time of exposure (Fabry and Buisson, 1913; Harrison, 1924; Twymann and Allsop). However, as it is not possible to make the lines under comparison to be of the same density purely by an adjustment of the calibrated drum, they were made as nearly equal as possible consistent with the accuracy of setting on the drum and the resulting images compared. Under such conditions, it is obvious that the photographic error introduced is a minimum.

In the case of diamond, the specimen could be held at the spark gap itself thereby ensuring proper alignment without much difficulty. In the case of the three crystals, namely, calcite, barytes and gypsum, investigated here, the scattering was comparatively weaker and it was found that the scattered light had to be focussed on the spark gap after adjusting the specimen to be in a line with the collimator of the spectrograph and the Spekker

photometer. But the choice of the condensing lens was determined by the condition that the divergence of the beam should be sufficient to make the scattered light falling on the quartz rhombs to be of uniform intensity. Though fairly big crystals were employed, only a small portion of the crystal was in focus at the spark gap.

Since the comparison was made between one line (approximately) at λ 2460 and another at λ 2625, it was necessary that the specimen employed should be free from all trace of colour and should not exhibit increased absorption at the shorter wavelengths. This correction for differential absorption is obviously different from that necessary when the exciting radiation is close to one of the characteristic ultraviolet absorption frequencies. For gypsum this effect was negligible. In the case of barytes and calcite, however, the absorption in the λ 2460 region was slightly higher than that in the λ 2625 region. The relative absorption in the two regions were therefore estimated by using the Spekker photometer and the correction necessary was found to be about 5% for barytes and for 8% for calcite. The intensity ratios of the Stokes—to the anti-Stokes component of the principal Raman lines of gypsum, barytes and calcite are given in Table I.

TABLE I

Crystal	Frequency shift of the line in cm.$^{-1}$	$e^{\frac{h\nu_i}{kT}}$	$\left(\frac{\nu-\nu_i}{\nu+\nu_i}\right)^4$	$e^{\frac{h\nu_i}{kT}}\left(\frac{\nu-\nu_i}{\nu+\nu_i}\right)^4$	Experiment
Gypsum ..	1006	121·6	·815	99	92·3
Barytes ..	988	115	·818	93·8	97
Calcite ..	1085	183·1	·802	147	151

The theoretical formula for the ratio of intensity of the Stokes and anti-Stokes components is given by $e^{\frac{h\nu_i}{kT}}\left(\frac{\nu-\nu_i}{\nu+\nu_i}\right)^4$ where the Boltzmann factor is predominant for lines with frequency shift less than 600 cm.$^{-1}$ It is obvious from the figures given in Table I that the method used here enables not only to study the high-frequency Raman lines, but also offers an invaluable means of confirming the dependence of the intensity on the fourth power of the emission frequency.

The author wishes to express his grateful thanks to Professor R. S. Krishnan for his kind interest in the work and to Professor N. Seetharaman of Presidency College, Madras, for the loan of the Spekker photometer.

SUMMARY

The relative intensities of the Stokes and anti-Stokes components of the most intense and high frequency shift Raman lines in calcite, gypsum, and barytes have been studied by a spectrophotometric method and the results confirm the dependence of the intensity of a Raman line on the fourth power of the emission frequency.

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THE STRUCTURE OF PECTIN

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Received September 27, 1949

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Theories on the structure of pectin have developed on much the same lines as in the case of other polysaccharides, conceptions postulating the aggregation of small molecules into colloidal micelles having given place to structures based upon the existence of macro-molecules.

According to the classical view pectin was considered to be built up of 6 mono-saccharide units consisting of 4 partially methoxylated galacturonic acid residues and 1 molecule each of arabinose and galactose. Based upon the earlier work of Ehrlich (1917, 1926, 1928 and 1929) and von Fellenberg (1918) and following improvements on the estimation of pectin, uronic acid and pentoses introduced by Carre, Ling, Schryver and others Nanji, Paton and Ling (1925) advanced the view that the basic structural unit of pectin was a pectic acid consisting of 4 galacturonic acid residues together with 1 residue each of arabinose and galactose, the 6 units being arranged in the form of a hexagonal ring; pectin itself was considered to be a completely methylated ester of pectic acid. The formula proposed by Nanji, *et al.* (1925) was later deprived of its chief experimental basis when Norris and Resch (1935) demonstrated that the calculations of the yield of furfual by Nanji, *et al.* (1925) were based upon incorrect assumptions. It became completely untenable when Link, *et al.* (1934) isolated from the partial degradation products of pectin, a polygalacturonide which was shown to contain 8 to 10 galacturonic acid residues. Studies on the configuration of the galacturonic acid units by the method of exhaustive methylation (Luckett and Smith, 1940; Smith, 1939) indicated a 1 : 4 α-glycosidic structure similar to that of starch. From osmotic measurements Luckett and Smith (1940) concluded that the pectic acid molecule contained 13 units.

However evidence for a much greater molecular magnitude and a cellulose-like rather than starch-like configuration was adduced by Schneider and co-workers (1936, 1937). The difficulties inherent in making reliable osmotic and cryoscopic measurements of aqueous solutions of complex

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colloidal substances which had previously led to low molecular weights were avoided by these authors by carrying out their studies on solutions of nitro, acetyl and formyl esters of pectin in non-polar solvents. The result of an intensive study of the physico-chemical properties of these esters was to prove that pectin is a filiform macro-molecule with a molecular weight of the order of 30,000 to 100,000, in conformity with ultra-centrifugal measurements on pectin from various sources (Norris, 1938). A comparison of the physico-chemical properties of the esters of cellulose, starch and pectin showed that in structure the pectin molecule resembled cellulose rather than starch.

Schneider and Bock (1937) also produced evidence in favour of the view that arabinose and galactose were not integral parts of the pectin molecule by preparing pectin containing neither of these sugars by a simple modification of the usual purification by fractional precipitation. By this means it was found possible to obtain from crude citrus pectin preparations of pectin containing 92·5% galacturonic acid and 11·4% methoxyl. Similar preparations were obtained from orange and apple pectins.

From the evidence at present available it is clear that the essential structural basis of the pectin molecule is a long chain of galacturonic acid units glycosidically linked to each other, and with some of the carboxyls esterified with methyl groups. This new conception of pectin structure raises many important questions, some of which are: (1) the freedom from arabinose and galactose of pectin preparations obtained from different sources, (2) the identity of the basic structural units in different pectins and (3) the chain length of the molecule. The present paper gives an account of experiments carried out with reference to these questions on pectins from pumpkin, guava, country pears and pomelo the preparation of which was described in a previous communication (Damodaran and Rangachari, 1945).

Experimental

Purification of pectin.—The preparations of pectin described previously were purified according to the method of Schneider and Bock (1937) by repeated precipitation with decreasing strengths of alcohol. The crude product in each case was submitted to 3 precipitations, once with 70% alcohol then with 60% alcohol and finally with 50% alcohol. Analytical values for uronic acid and methoxyl though high, ranging as they did from 82 to 86% uronic acid and 8·1 to 9·7% methoxyl, showed that the products dealt with were not entirely of the nature of polyuronides. The purification experiments were therefore carried out in a more systematic manner, precipitation with alcohol at any particular strength being repeated till constant analytical values were obtained.

The crude samples were dissolved in hot water, repeatedly filtered through paper pulp to remove turbidity and the filtrate precipitated with alcohol added to a final concentration of 70%. The material so obtained was analysed for its uronic acid content according to the method of Dickson, Otterson and Link (1930) and for methoxyl by the usual micro-Zeisel method (Pregl, 1937). This material was redissolved after analysis and subjected to reprecipitation with alcohol of the same concentration. This procedure was repeated till the uronic acid and methoxyl values became practically constant; usually 3 precipitations were found necessary. The material so obtained was again dissolved in water, filtered and now precipitated with alcohol added to a final concentration of 60%. Reprecipitations with 60% alcohol were carried out as before and the material of constant composition was then subjected to repeated precipitation with alcohol of 50% final concentration. At each stage, the samples were analysed for their uronic acid and methoxyl contents; the results are tabulated below.

TABLE I

Material	70%		60%		50%	
	1st Pptn.	3rd Pptn.	1st Pptn.	3rd Pptn.	1st Pptn.	3rd Pptn.
Pumpkin (*Cucurbita pepo*)						
Galacturonic acid % ..	55·12	65·37	76·56	84·18	90·12	92·16
Methoxyl % ..	5·24	6·41	7·25	7·98	9·82	10·87
Pomelo (*Citrus pomelo*)						
Galacturonic acid % ..	67·27	72·39	80·18	87·55	91·27	92·57
Methoxyl % ..	6·92	7·25	8·39	9·21	10·56	11·05
Guava (*Psidium guava*)						
Galacturonic % ..	76·48	79·37	85·92	89·11	93·25	93·26
Methoxyl acid % ..	7·84	8·21	9·52	9·85	10·57	10·57
Country pears (*Pyrus communis*)						
Galcturonic acid % ..	62·08	73·21	82·64	85·47	91·52	91·64
Methoxyl % ..	7·69	8·92	10·63	10·85	11·97	12·02

It is obvious from the above table that on repeated precipitation from alcohol of decreasing strength there is a progressive fall in the impurities that are present in the preparations and the uronic acid tends to a value pertaining to that of a polyuronide. There cannot be much doubt from the results that arabinose and galactose are not essential constituents of pectin but are derived from impurities, arabans and galactans, which are difficult to remove on account of the similarity of their solubility properties to those of pectin. The fact that uronic acid and methoxyl values obtained are in good agreement with each other and with those of Schneider, *et al.*

(1937) makes it highly probable that all the preparations contain an identical pectin molecule.

As this question could not be settled by the preparation of completely pure pectin on account of the difficulty of removing all traces of adherent polysaccharides by fractional precipitation resort was had to the preparation of the basal pectic acid from the different raw materials investigated.

Preparation of the basal pectic acid.—The crude pectin sample was dissolved in sodium hydroxide solution, filtered to remove any undissolved material and the solution left overnight for de-esterification to be complete. It was then treated with dilute hydrochloric acid when the insoluble pectic acid was precipitated as a jelly. The pectic acid was filtered off, washed repeatedly with water to remove acid, then dehydrated by washing with alcohol and finally with acetone. The material thus obtained was dried *in vacuo* and analysed for its uronic acid content. The values obtained (Table II) are seen to be much lower than for a polygalacturonic acid. Evidently in this method of preparation the accompanying polysaccharides are co-precipitated with the pectic acid.

Therefore, following Link and Nedden (1931–32) the calcium-sodium pectate was first precipitated and the free pectic acid liberated from this by treatment with acid. The pectin extract obtained by boiling the minced fruit material with N/75 hydrochloric acid was directly treated with calcium oxide, a 10% suspension of the latter in water being added to a pH of 8·5 to 8/9. 200 ml. of N/10 sodium hydroxide at 37° were then added and the mixture maintained at a temperature of 37°–40° for 10 minutes when a jelly-like material separated. The precipitate was centrifuged off, washed with water to remove alkali and treated finally with dilute hydrochloric acid to convert the salt into the free acid. The precipitate was then washed with water till free from chloride, dehydrated with alcohol and dried *in vacuo*. The pectic acid from the 4 different materials thus obtained had a uronic acid content of 97 to 98% (Table II) and was obviously a compound made up almost entirely of galacturonic acid residues. The values are also sufficiently in agreement to conclude that the pectins from various sources have the same basic structure.

Calcium equivalent of pectic acid.—The calcium salt formed by demethylated pectin is known to be a definite chemical compound (Nanji, *et al.*, 1925; Hinton, 1939) and can be precipitated under conditions precluding interference by any organic acid or other compounds likely to be present in plant materials. It is also possible to estimate the percentage of calcium in this precipitate with great accuracy by the simple process of incineration.

TABLE II

Material	% Uronic Acid		
	Pectin	Pectic acid	
		By usual precipitation	Link's method
Lemon Peel ..	75·48	84·48	97·69
Pomelo Peel ..	54·68	80·52	98·54
Guava ..	50·44	68·96	97·39
Pumpkin ..	51·74	69·16	98·27
Country pears ..	54·72	76·44	98·12

The equivalent weight of pectic acid which can be calculated from this value provides a basis for assessing the chemical homogeneity of pectin prepared from different sources. If pectin is assumed to be a partially methylated polygalacturonide the equivalent weight of pectic acid derived from it should lie between narrow limits and the actual value will depend upon the size of the molecule. If 'n' galacturonic acid units combined in glycosidic linkage are present, then the weight of the pectic acid molecule will be $194n - (n - 1)\ 18$ with 'n' free carboxyl groups. Thus its equivalent weight (weight combining with one equivalent of calcium) would be $\frac{194\,n - (n-1)\,18}{n}$ and each gram of substance would give rise to $\frac{50{\cdot}04 \times n}{194n - (n-1)\,18}$ g. of calcium carbonate in the calcium estimation. Table III gives the

TABLE III

No. of galacturonic acid units	Equivalent weight of pectic acid	Yield of calcium carbonate per g. of pectic acid
1	194·00	0·2577
4	180·50	0·2770
8	178·25	0·2805
10	177·80	0·2812
50	176·36	0·2834
100	176·18	0·2839

equivalent weight and weight of calcium carbonate per gram of pectic acid calculated for various chain lengths according to the above formula. It is apparent that an estimation of calcium according to the usual methods should give a reliable indication of the size of the pectic acid molecule upto a chain length of the order of 50 to 100 units.

Determinations of the calcium equivalent were carried out on pectin preparations purified as described above. About 1 g. of the purified pectin was weighed out accurately, dissolved in distilled water and made upto 100 ml. 20 ml. aliquots were pipetted out and calcium pectate was precipitated from this solution according to Carre and Haynes (1922). This was filtered through quantitative filter-paper and repeatedly washed with hot water till the washings were free from chloride. The calcium content of the precipitate was estimated in the usual way be incineration to carbonate.

TABLE IV

Material	Weight taken g.	Methoxyl %	Wt. of pectic acid g.	Yield of $CaCO_3$ g.		Equal weight of pectic acid
				Actual	Per g.	
Pomelo ..	1·064	11·05	1·0109	0·2867	0·28361	176·27
Pumpkin ..	1·014	10·87	0·9462	0·2737	0·28386	176·27
Guava ..	1·0068	10·57	0·9587	0·2722	0·28393	176·23
Country pears ..	1·0285	12·02	0·9727	0·2761	0·28385	176·21

It can be seen from the above table that pectic acid preparations from pectins isolated from different sources are chemically indistinguishable from each other. The values for the equivalent weight of pectic acid calculated from the calcium content indicate a chain length of not less than 50 units, individual values showing a chain length of the order of 100 units. This is contrary to the findings of Luckett and Smith (1940) who on the basis of "end group assay" assigned to pectic acid a chain length of 13 galacturonic acid residues.

SUMMARY

Pectin from pumpkin, guava, country pears and pomelo has been purified by repeated fractional precipitation with decreasing strengths of alcohol according to the method of Schneider and Bock. The analytical values for uronic acid and methoxyl content show that neither arabinose nor galactose are integral constituents of pectin. The values also indicate the probability that the preparations contain an identical pectin molecule.

The identity of the basic structural unit has been confirmed by analysis of the pectic acid derived from the pectins from the 4 sources mentioned above, as well as by determination of the equivalent weights of the pectic acid by analysis of the calcium salt.

The equivalent weights found indicate that the chain length of the pectic acid molecule is of the order of 50 to 100 galacturonic acid units.

The author's grateful thanks are due to Prof. M. Damodaran for his guidance and advice.

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NUCLEAR RESONANCE IN FLOWING LIQUIDS

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Received December 2, 1950

(Communicated by Prof. R. S. Krishnan, F.A.SC.)

1. Introduction

Nuclear magnetic resonance is associated with relaxation phenomena (Bloembergen, Pound and Purcell, 1948). The relaxation effects for any given substance are described by means of two relaxation times T_1 and T_2. T_1 is the measure of the rate of attainment of thermal equilibrium of a system of nuclei in a magnetic field. T_2 is the inverse line breadth on a frequency scale and is otherwise called the spin-spin relaxation time. On account of the finite and fairly large (10^{-4} to 3 sec.) magnitudes of T_1 and T_2, several effects such as the saturation of the sample by R.F. field take place. In this paper experiments are described in which the saturated sample is continuously replaced by flow of a liquid, through the R.F. coil of the apparatus. On account of the large value of the relaxation time, even moderate velocities of flow are sufficient to cause several interesting features to be observed which are described below.

2. Apparatus

In order to show the effects clearly an easily adjustable and sensitive apparatus for detecting nuclear resonance is necessary. It has been found that the self-quenched superregenerator satisfies the requirement of simplicity and sensitiveness. The circuit used functions at radio frequencies ranging from 1 to 20 M.C./s. with a quench frequency of 20 K.C./S. The oscillator coil is wound on a glass former and is capable of being placed with its shield within the $\frac{3}{4}''$ gap of an electromagnet. The magnet pole-pieces are of the truncated pyramid type and have a pole face area $3'' \times 3''$. The main exciting coils are of thin wire and at a current of 1·5 amperes through them, a field of 6,000 oersteds can be obtained in the $\frac{3}{4}''$ air gap. An extra pair of coils are provided through which a 60 cycle alternating current of magnitude 1 to 3 amperes can be sent by means of a transformer. The audio output of the superregenerator is fed to a Cossor oscillograph whose linear sweep is synchronized with the 60 cycles mains frequency.

Through the R.F. coil passes one limb of a U tube which is connected to the liquid flow system. An arrangement to reverse the flow is also provided. The liquid is kept in a small reservoir at a height of 50 cm. above the R.F. coil and is allowed to flow by gravity.

3. Experimental Details

Experiments will now be described which show the phenomenon of nuclear magnetic resonance relaxation in a very striking manner. The magnetic field is adjusted for obtaining resonance. The flow system should be filled with a liquid or a solution having a fairly large relaxation time of the order of 0·1 to 0·05 sec. in order to exhibit the effects. When the liquid is stationary a signal of about 1 cm. height on the screen of the oscillograph is observed. On flowing the liquid two most striking effects are noticed. Firstly, there is a large temporary rise in signal strength which subsides quickly. Secondly, there is the relatively larger signal obtained when the liquid is flowing steadily. The magnitudes of these effects are conditioned by various factors, *viz.*, the relaxation time T_1 of the liquid, the time it spent in the magnetic field outside the R.F. field, the time it spends in the R.F. coil and the velocity of flow. Initial rises in signal of magnitudes 20 times the no-flow signal value have been observed. Steady flow to no-flow signal ratio are usually about 5 and are dependent on the velocity of flow. The observed results in a particular case are represented in the accompanying graph.

4. Discussion

The experiments mentioned above form a striking demonstration of the facts of nuclear magnetic relaxation. The effects are all quantitatively related to the relaxation time. The finite and long relaxation time leads as mentioned earlier to a saturation of the sample and the saturation is expressed quantitatively by the ratio

$$\frac{n}{n_0} = \frac{1}{1 + \gamma^2 T_1 T_2^* H_1^2},$$

where T_1 is the relaxation time, T_2^* is the inverse line breadths (on the frequency scale) γ the gyromagnetic ratio of the nuclei, H_1 is the effective R.F. magnetic field; and n/n_0, the ratio of the excess number of nuclei in the higher state with and without the R.F. R.F. absorption is proportional to n. In flowing the liquid we have removed the saturated sample and replaced it by unsaturated sample capable of absorbing more R.F. energy resulting in a larger signal.

The first effect described above is the initial rise in signal. This could be observed under the following conditions. (1) The liquid should have a long relaxation time of the order of 0·1 sec. or more. (2) It must come to thermal equilibrium in the magnetic field; *i.e.*, it must have spent a time considerably larger than the relaxation time in the magnetic field at or near the resonance value. (3) It must travel with sufficient velocity to displace the contents of the R.F. coil in a time of the order of 1/120 sec. A simple relation between the rise and the relaxation time can be obtained. Assuming that the signal is proportioned to the excess number of nuclei in the lower state, we have

$$\frac{n}{n_0}=\frac{s}{s_0}=\frac{1}{R}=\frac{1}{1+\gamma^2 T_1 T_2^* H_1^2}$$

R being the ratio of the steady signal s to the initial rise s_0. Then

$$\frac{R-1}{\gamma^2 T_2^*}=T_1 H_1^2.$$

If H_1 could be measured, T_1 can be calculated by performing this experiment. However, the direct determination of H_1 is difficult and only a comparison of T_1 between liquids can be effected.

Secondly, there is a rise in signal when the liquid is flowing steadily with a uniform velocity. Here the conditions of observation are the following: (1) The relaxation time must be of the order of 0·1 to ·01 sec. (2) The liquid must travel for sufficient time in the magnetic field before entry into the R.F. coil for attaining thermal equilibrium. (3) It must travel with sufficient velocity to displace at least a part of the contents of the R.F. coil in a time of the order of 1/60 sec. For these moderate velocities it is possible to calculate the steady state rise. It will suffice to give the results of the calculation. If l is the length of the R.F. coil, v the velocity of flow, T_1 the relaxation time, s_0 the signal when the liquid is at rest and s the signal when the liquid is flowing, then

$$\frac{s-s_0}{s_0}=\frac{WT_1^2}{1+WT_1}\times\frac{v}{l},$$

where

$$W=\tfrac{1}{2}\gamma^2 H_1^2 T_2^* \text{ and if } WT_1 \text{ is large}$$

$$\frac{s-s_0}{s_0}=T_1\frac{v}{l} \text{ approximately.}$$

This also affords a method of estimating the relaxation time T_1. Fig. 1 shows an experimental curve for N/1,000 $FeCl_3$ solution and T_1 given by the slope of the curve is 0·06 sec.

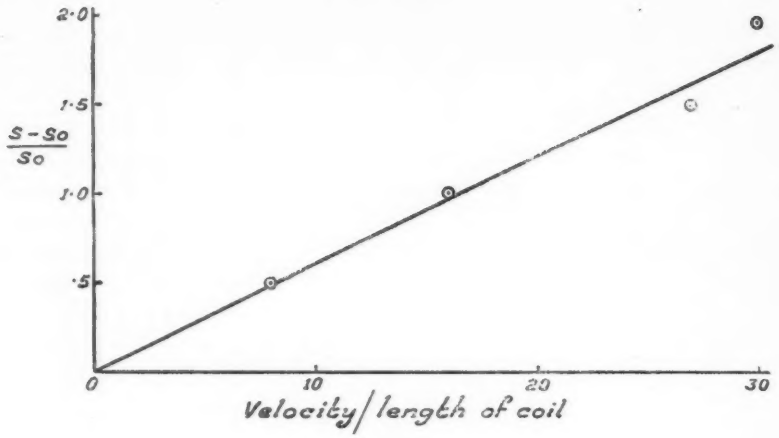

FIG. 1

There is another possibility of steady state rise under conditions described in case 1 above. If the liquid is allowed to flow steadily, then the time it spends outside the R.F. field but still in the magnetic field is small and the liquid will not come to proper thermal equilibrium. Therefore the signal on steady flow will not be as large as the initial rise. Here the rise is determined by the time the fluid travels in the magnetic field before entry into the R.F. field.

These experiments afford a clear demonstration of relaxation time and saturation in nuclear magnetic resonance and offer a unique method of answering questions regarding the behaviour of nuclei within and without the R.F. field. One of the questions is whether the time taken to come to thermal equilibrium in a magnetic field is the same as the time taken to come to thermal equilibrium in the presence of an R.F. field also. Experiments have been performed which answer the question in the affirmative.

Another question is whether the free precession of the nuclei after they have left the R.F. field could be detected. Experiments have been performed by placing a pick up loop on the return limb of the U tube through which the liquid flows and connecting the loop to a highly sensitive communications receiver. If the liquid is flowed and the nuclei are precessing coherently, the output of the receiver must change. With $FeCl_3$ solutions used and the velocities obtained, no definite change could be observed. This, however, is not surprising in view of the fact that the phase memory time T_2 is small and the magnetic field inhomogeneity contributes to make

it still smaller. If as is suspected, fluids exist with T_2 of the order of 0·1 sec. or more the above mentioned experiment will yield positive results.

I thank Professor R. S. Krishnan for his kind interest and encouragement.

Summary

Nuclear magnetic resonance in flowing liquids has been investigated experimentally. The experiments afford a striking demonstration of the effects of finite relaxation time and afford a method of measuring relaxation times directly.

Reference

1. Bloembergen, Pound and Purcell .. *Phys. Rev.*, 1948, **73**, 679.

FLAVONES: A DIRECT SYNTHESIS OF 6-HYDROXY-FLAVONES

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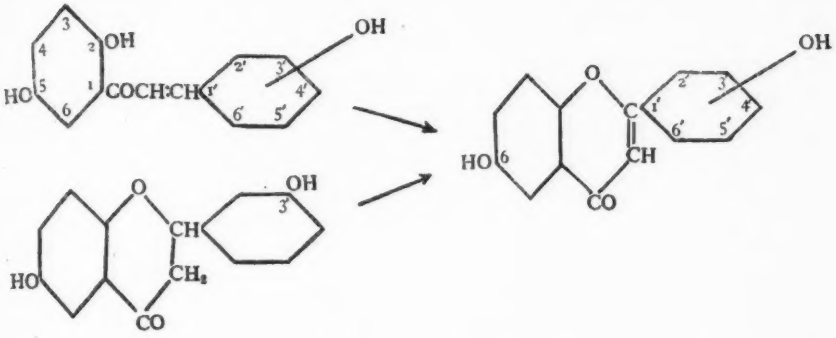
Received July 24, 1950

(Communicated by Dr. R. D. Desai, F.A.SC.)

A CONSIDERABLE amount of work has been done on the synthesis of flavones. Kostanecki and co-workers[1] synthesised several flavones starting with the bromination of flavanones or chalkones—a method involving several subsequent reactions—which sometimes led to the formation of the nuclear bromination products or benzal-coumaranones instead of the expected flavones.[2]

Venkataraman and co-workers[3] introduced the use of selenium dioxide for the direct oxidation of *o*-hydroxy-chalkones to the flavones. The Venkataraman oxidation is elegant, simple and leads to no complications. Thus they synthesised benzyloxy-flavones from the corresponding *o*-hydroxy-benzyloxy-chalkones. Later on selenium dioxide was tried unsuccessfully to oxidise chromanones to chromones.[4] These unsuccessful efforts created a doubt about the applicability of this reagent to the oxidation of chalkones also. But Chakravarti and Dutta[4] were successful to oxidise chloro- and nitro-derivatives of 2-hydroxy-3′-4′-dimethoxy chalkones to the corresponding flavones with good yields. Seshadri and co-workers[5] have remarked that the use of selenium dioxide has been found satisfactory only in a few simple cases and it seems to fail when the chalkone contains a number of free hydroxy groups. They have used iodine as a dehydrogenating agent with limited application only to flavanones containing hydroxy group in 5-position.

In connection with our work on chalkones and flavanones derived from quinacetophenone,[6] we have satisfactorily employed selenium dioxide as oxidising agent for the synthesis of 6-hydroxy-flavones directly from the corresponding hydroxy-chalkones. 2:5-Dihydroxy-, 2:5:2′-trihydroxy-, 2:5:4′-trihydroxy-chalkones as well as 6:3′-dihydroxy-flavanone have been successfully oxidised to the corresponding 6-hydroxy-flavones. The yields of 6-hydroxy-flavones, however, were poor.



It is interesting to note that in the present work, selenium dioxide has been applied as an oxidising agent to convert *o*-hydroxy-chalkones containing free hydroxy groups into the corresponding flavones. It possibly establishes the general applicability of selenium dioxide for the direct synthesis of the hydroxy-flavones from the corresponding *o*-hydroxy-chalkones or flavanones. The synthesis of 6-hydroxy flavones by Kostanecki and coworkers involved five steps, (i) alkylation of the ketone and aldehyde, (ii) formation of flavanone or chalkone, (iii) bromination of flavanone or acetoxy chalkone, (iv) action of alcoholic potassium hydroxide on the bromo compound and (v) dealkylation of the final flavone: on the other hand, in the present work, the flavones have been synthesised in one step. These flavones gave acetyl derivatives agreeing with Kostanecki's products. They also give greenish-yellow fluorescence in concentrated sulphuric acid and dissolve in sodium hydroxide with yellow colouration.

Experimental

6-*Hydroxy-flavone*

2: 5-Dihydroxy-chalkone (1 g.) was dissolved in dry freshly distilled amyl alcohol (20 c.c.), selenium dioxide (2 g.) added and the mixture refluxed on oil-bath at 140–50° for 10 to 12 hours. The hot solution was filtered from metallic selenium. The filtrate on cooling deposited pale red crystals which were recrystallised from dilute alcohol, colourless needles, m.p. 234°. Kostanecki, Levi and Tambor (*Ber.*, 1899, 32, 331) give the m.p. 232°.

The acetyl derivative was prepared by refluxing the flavone (0·3 g.) with acetic anhydride (2 c.c.) and sodium acetate (0·5 g.) for 3 hours on water-bath. It was then treated with ice-water. The solid that separated was crystallised from dilute alcohol, long colourless shining needles, m.p.

158°. Kostanecki, *et al.* (*loc. cit.*) give the same m.p. (Found: C, 72·6; H, 4·4; Calculated for $C_{17}H_{12}O_4$: C, 72·8; H, 4·3 per cent.).

6: 2′-*Dihydroxy-flavone*

A mixture of 2: 5: 2′-trihydroxy chalkone (2 g.), amyl alcohol (30 c.c.) and selenium dioxide (2 g.) was refluxed on oil-bath at 140–50° for 10–12 hours and then filtered from the precipitated selenium and amyl alcohol removed by steam-distillation; fine pale red powder obtained was crystallised from alcohol, pale red microcrystals, unmelted upto 290°. Kostanecki and Seifart (*Ber.*, 1900, *33*, 2509) give m.p. 305° (Found: C, 70·8; H, 3·7; Calculated for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9 per cent.).

The acetyl derivative prepared as before crystallised from alcohol, colourless needles, m.p. 148°. Kostanecki and Seifart (*loc. cit.*) give the same m.p. (Found: C, 67·5; H, 4·1; Calculated for, $C_{19}H_{14}O_6$: C, 67·5; H, 4·1 per cent.).

6: 4′-*Dihydroxy flavone*

2: 5: 4′-Trihydroxy-chalkone was oxidised as in the previous case. After removal of amyl alcohol by steam distillation, it was continued further when a solid began to appear in the distillate. It was extracted with ether; after the removal of ether, pale yellow solid obtained was crystallised from alcohol, pale yellow microcrystalline substance unmelted upto 300°. Kostanecki and Oderfield (*Ber.*, 1899, 32, 1929) record the m.p. 320°. (Found: C, 71·0; H, 3·8; Calculated for $C_{15}H_{10}O_4$: C, 70·9; H, 3·9 per cent.).

The acetyl derivative prepared as above crystallised as colourless needles from dilute acetic acid, m.p. 208°. Kostanecki and Oderfield (*loc. cit.*) give the same m.p. (Found: C, 67·3; H, 4·0; Calculated for $C_{19}H_{14}O_6$; C, 67·5; H, 4·1 per cent.).

6: 3′-*Dihydroxy flavone*

6: 3′-Dihydroxy-flavanone (1 g.) was oxidised in the same manner as before; pale yellow needles, m.p. 300°, were obtained from alcohol. Kostanecki and Blumstein (*Ber.*, 1900 *33*, 1478) record the same m.p.

The acetyl derivative prepared as above, crystallised from alcohol, colourless needles, m.p. 170°. Kostanecki and Blumstein (*loc. cit.*) record the same m.p. (Found: C, 67·3; H, 4·2; Calculated for $C_{19}H_{14}O_6$: C, 67·5; H, 4·1 per cent.).

SUMMARY

6-Hydroxy-flavones have been synthesised by the Venkataraman oxidation of 2: 5-dihydroxy-, 2: 5: 2′-trihydroxy-, 2: 5: 4′-trihydroxy chalkones as

well as 6:3′-dihydroxy-flavanone by selenium dioxide. Thus the poly-hydroxy-chalkones can be oxidised to the corresponding hydroxy-flavones in one step.

References

1. Kostanecki and co-workers — *Ber.*, 1898, **31**, 696, 705, 1757; 1899, **32**, 326; 1900, **33**, 322, 1478, 2509.
2. ——— and Tambor .. *Ibid.*, 1899, **32**, 2263.
   Cullinane and Phillpott .. *J. C. S.*, 1929, 1761.
   Mahal and Venkataraman .. *Ibid.*, 1936, 569.
3. Venkataraman and co-workers — *Ibid.*, 1935, 866; 1936, 569.
4. Chakravarti and Dutta .. *J. I. C. S.*, 1939, **16**, 639.
5. Seshadri and Narasimhachari *Proc. Ind. Acad. Sci*, 1949, **30** A, 151.
6. Vyas and Shah .. *J. I. C. S.*, 1949, **26**, 273.

SYNTHETICAL EXPERIMENTS IN THE CHROMONE GROUP

Part XXIV. A Synthesis of Prunetin

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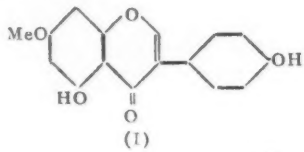
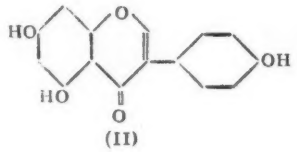
(From the Department of Chemical Technology, University of Bombay)

Received November 16, 1950

The first natural colouring matter to be recognized as an isoflavone was prunetin, isolated by Finnemore.[1] It occurs as the glucoside, *prunitrin*, in the bark of a variety of *Prunus*, probably *Prunus emarginata*, used as a substitute for the bark of *Prunus serotina*. Finnemore found that prunetin, $C_{16}H_{12}O_5$, contained one methoxyl and two hydroxyl groups; fusion with caustic potash at 250° gave *p*-hydroxyphenylacetic acid and a phenol which responded to the colour reactions of phloroglucinol and which yielded methyl iodide on treatment with hydriodic acid. Methylation gave a monomethyl ether, and demethylation with hydriodic acid gave prunetol, $C_{15}H_{10}O_5$, which formed a yellow sulphate ($C_{15}H_{10}O_5$, H_2SO_4) with sulphuric acid. On the basis of these results, Finnemore concluded that prunetin was 5 : 4′-dihydroxy-7-methoxy-isoflavone (I) and prunetol 5 : 7 : 4′-trihydroxy-isoflavone (II).



(I)



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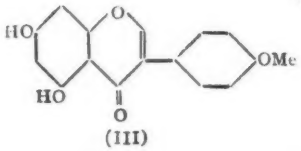
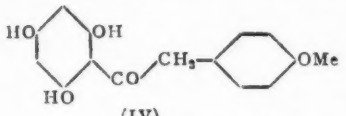


(III)

Following a suggestion made by A. G. Perkin that prunetol was probably identical with genistein, the colouring matter of Dyer's Broom (*Genista tinctoria*) and one of the isoflavone constituents of soya beans (*Soja hispida*), Baker and Robinson[2] made a direct comparison and proved their identity. They also synthesized 5-hydroxy-7 : 4′-dimethoxy-6-methylisoflavone (methylgenistein dimethyl ether) by a series of reactions involving the preparation of a 2-styrylisoflavone, its oxidation to the 2-carboxylic acid and final decarboxylation. The fact that several isoflavones (*e.g.*, genistein)

occur in nature as glycosides in which the sugar residue is attached to a hydroxyl in the 7-position led Robinson[3] to suggest that prunetin was perhaps the 4′-methyl ether (III) of prunetol. More recently, Shriner and Hull[4] have reported the synthesis of genistein 4′-methyl ether (III) by treating 2:4:6-trihydroxyphenyl 4-methoxybenzyl ketone (IV) with sodium and ethyl formate, utilizing the procedure of Joshi and one of us[4]; (III) was different in its properties from prunetin, so that prunetin must be constituted as genistein 7-methyl ether (I).

Biochanin-A, one of the substances isolated by Siddiqui[5] from sprouted gram (*Cicer arietinum* Linn.) was formulated by Bose and Siddiqui as the 4′-methyl ether (III) of genistein. The m.p. of the compound agrees with that quoted by Shriner and Hull[4] for synthetic (III).



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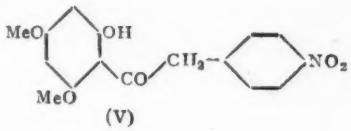

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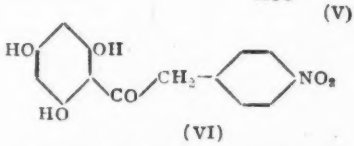
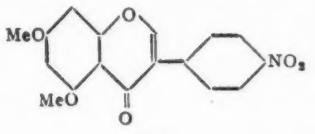


(VI)

No attempts on the synthesis of 5:4′-dihydroxy-7-methoxyisoflavone (I) have been recorded. In the present work a method has been developed for the synthesis of (I) and it promises to be useful for the synthesis of other partially methylated polyhydroxyisoflavones.

α-Naphthaisoflavone was obtained by Sathe and one of us[6] by the action of ethyl orthoformate, pyridine and piperidine on 2-phenylacetyl-1-naphthol. The application of this reaction to 2-hydroxy-4:6-dimethoxyphenyl 4-nitrobenzyl ketone (V), obtained by the action of diazomethane on 2:4:6-trihydroxyphenyl 4-nitrobenzyl ketone (VI),[7] gave a compound which did not exhibit a ferric chloride coloration, was insoluble in cold



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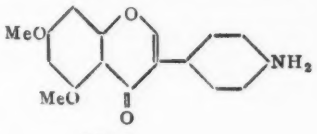

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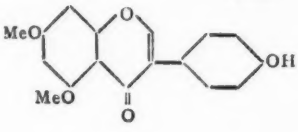
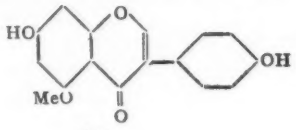


(IX)

caustic soda solution and analysed correctly for 5:7-dimethoxy-4′-nitroisoflavone (VII).[8] The compound (VII) was reduced to the amine (VIII) by iron powder or zinc dust in boiling alcohol-acetic acid. Diazotization of (VIII) and hydrolysis of the diazonium salt yielded 4′-hydroxy-5:7-dimethoxyisoflavone (IX), obtained earlier by Zemplen, *et al.*[9] by methylation and acid hydrolysis of sophorabioside and sophoricoside, the isoflavone glycosides in *Sophora japonica*, L.; there is complete agreement in the behaviour of (IX) and Zemplen's compound.

Preferential demethylation of the 5- or 3-methoxyl group in flavones and flavonols can be effected by means of aluminium chloride in nitrobenzene or hydrobromic acid in acetic acid.[10] This technique of partial demethylation, since used for the synthesis of several naturally occurring flavones and flavonols, has now proved to be of value in the isoflavone series. Preferential demethylation of (IX) in the 5-position by means of aluminium chloride



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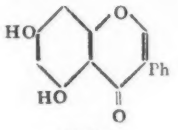
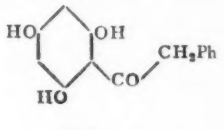


(XI)

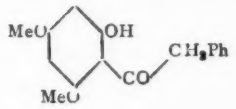


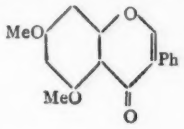
(XII)

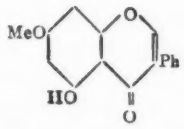
in nitrobenzene afforded 5-4′-dihydroxy-7-methoxyisoflavone (I), which had all the properties of prunetin described by Finnemore.[1] Chakravarti and Bhar[11] isolated an isoflavone, prunusetin, together with puddumetin or genkwanin (5:4′-dihydroxy-7-methoxy-flavone) from the bark of the Indian wild cherry (*Prunus puddum* Roxb.; Hindi: *Padam*). From a study of its behaviour towards methylating agents, prunusetin was considered to be genistein 5-methyl ether (X). Narasimhachari and Seshadri[12] later re-examined prunusetin and showed that it was a slightly impure sample of prunetin. We have found that prunusetin and its diacetate are identical in all respects with synthetic (I) and its diacetate; the samples kindly supplied by Dr. D. Chakravarti melted more sharply and had melting points nearer our synthetic specimens than those kindly supplied by Professor T. R. Seshadri. Thus there is no doubt regarding the identity of prunetin and prunusetin, and the latter name may now be abandoned.

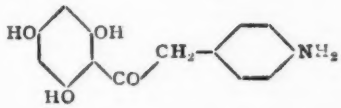
Späth and Lederer[13] synthesized the naturally occurring isoflavones, daidzein and pseudobaptigenin, by condensing the appropriate benzyl *o*-hydroxyphenyl ketone with ethyl formate and sodium at 100° in a sealed tube, treating the product with boiling alcoholic hydrochloric acid and purifying by high vacuum sublimation. It was later observed by Joshi and others[14] that the condensation of benzyl *o*-hydroxyphenyl ketones with ethyl

formate and sodium usually proceeds at 0° to yield the isoflavone in one stage. While these workers protected hydroxyl groups other than the 2-hydroxyl, Shriner and Hull found that this is not necessary in the synthesis of 5:7-dihydroxy-4′-methoxyisoflavone (Biochanin-A)[4] and 5:7:4′-trihydroxy-8-methylisoflavone (8-methyl genistein).[15] We find that the reaction can be carried out without protection of the 4-hydroxyl group in benzyl 2:4-dihydroxyphenyl ketone, although the 4-benzyl ether furnishes a better yield; but we have encountered difficulties in the preparation of 5:7-dihydroxyisoflavone (XI) directly from benzyl 2:4:6-trihydroxyphenyl ketone (XII). On the other hand, benzyl 2-hydroxy-4:6-dimethoxyphenyl ketone (XIII) condensed readily with ethyl formate and sodium to 5:7-dimethoxyisoflavone (XIV), and demethylation with hydriodic acid gave

(XIII) 

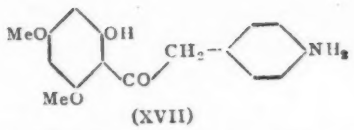
 (XIV)

(XV) 

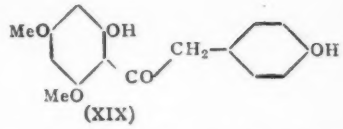
 (XVI)

5:7-dihydroxyisoflavone; partial demethylation with hydrobromic acid in acetic acid resulted in 5-hydroxy-7-methoxyisoflavone (XV).

2:4:6-Trihydroxyphenyl 4-nitrobenzyl ketone (VI), prepared according to Yamashita,[7] can be reduced to the corresponding amine (XVI) by the action of hydrogen at 40 lb. pressure in the presence of Raney nickel. The same amine was also obtained by the Hoesch reaction between phloroglucinol and *p*-acetamidobenzyl cyanide, deacetylation taking place during hydrolysis of the ketimine hydrochloride. The dimethyl ether (V) was prepared by the action of diazomethane on (VI) as stated earlier; other methods of methylation using potassium carbonate or caustic soda led to resinous substances. Reduction of (V) with Raney nickel and hydrogen gave the aminoketone (XVII), converted into the N-acetyl derivative (XVIII) by treatment with one mole of acetyl chloride in toluene at room temperature. When the amine (XVII) was dissolved in boiling dilute sulphuric acid and treated with sodium nitrite, it underwent simultaneous diazotization and hydrolysis, yielding 4-hydroxybenzyl 2-hydroxy-4:6-dimethoxyphenyl ketone (XIX). The latter compound was also prepared according to Zemplen and Bognar[9] by the Hoesch reaction on phloroglucinol dimethyl ether and *p*-hydroxybenzyl cyanide. Attempts to prepare isoflavones from (V),



(XVII)



(XIX)

(VI), (XVIII) and (XIX) by the action of sodium and ethyl formate under the conditions employed by Joshi, *et al.*[14] were unsuccessful, but in view of the ready accessibility of prunetin by an alternative route the reaction was not studied more thoroughly.

Experimental

2-Hydroxy-4: 6-dimethoxyphenyl 4-nitrobenzyl ketone

The ketone (VI) (2 g.), prepared according to Yamashita,[7] was dissolved in ether (100 c.c.) and mixed at 0° with an ether solution of diazomethane, prepared from nitrosomethylurea (4 g.). The mixture was kept in the refrigerator for 48 hours, and ether was then decanted off from the crystals that had separated. On recrystallization from alcohol, nearly colourless needles (1·25 g.), melting at 148°, were obtained (Found: C, 60·7; H, 4·8; N, 4·6. $C_{16}H_{15}O_6N$ requires C, 60·6; H, 4·7; N, 4·4%). The substance is insoluble in aqueous sodium carbonate, but gives a violet coloration with sodium hydroxide. The alcoholic solution gives a brown coloration with ferric chloride.

5: 7-Dimethoxy-4′-nitroisoflavone (VII)

The ketone (5 g.) was treated with dry pyridine (40 c.c.), when it became bluish red. On the adddition of piperidine (1·5 c.c.) the solution became violet. Ethyl orthoformate (30 c.c., 10 mols.) was added, when the solution became orange-red. The mixture was refluxed for 8 hours and allowed to stand overnight; the white crystalline precipitate (4·2 g.) was filtered, washed with *n*-hexane and crystallized from acetic acid in needles and melted at 220–22° (Found: C, 62·1; H, 4·2; N, 4·4. $C_{17}H_{13}O_6N$ requires C, 62·4; H, 4·2; N, 4·3%). Cyclization of the ketone (VI) to the isoflavone (VII) was indicated by the insolubility in aqueous caustic soda and the absence of ferric chloride coloration.

4′-Amino-5: 7-dimethoxyisoflavone (VIII)

5: 7-Dimethoxy-4′-nitroisoflavone (5·8 g.) and zinc dust (5·8 g.) suspended in boiling 50% alcohol (75 c.c.) and acetic acid (20 c.c.) was added in four portions at intervals of 30 minutes each. After refluxing for 30 minutes longer, the solution was filtered hot, the filtrate concentrated to 10 c.c. and diluted with water. The precipitate was collected (4·7 g.) On

crystallizing twice from alcohol, it was obtained as broken plates, m.p. 206°. Traces of unreduced nitro compound and intermediate products of reduction were apparently present. The substance was therefore dissolved in chloroform and saturated with dry hydrochloric acid; the white precipitate of amine hydrochloride was filtered, triturated with sodium bicarbonate solution, and filtered. The residue was then dissolved in chloroform and the chloroform solution filtered. The filtrate was evaporated to dryness on a water-bath and the residue twice crystallized from alcohol. The irregular plates, dried in vacuum at 120° for 5 hours, had m.p. 219–20° (Found: C, 68·1; H, 5·0; N, 4·9. $C_{17}H_{15}O_4N$ requires C, 68·7; H, 5·0: N, 4·9%).

4′-Hydroxy-5: 7-dimethoxyisoflavone (IX)

The amine (4·5 g.) was dissolved in a mixture of water (250 c.c.) and concentrated sulphuric acid (45 c.c.). The solution was cooled in ice and treated with solution of sodium nitrite (1·7 g.). After allowing the mixture to stand at 0° for 30 minutes, the excess nitrous acid was destroyed by the addition of urea. The diazonium solution was gradually poured into a boiling mixture of water (400 c.c.) and concentrated sulphuric acid (200 c.c.). There was a brisk effervescence due to evolution of nitrogen, and after two minutes no red colour was obtained with alkaline β-naphthol, indicating the complete decomposition of the diazonium salt. The mixture was cooled and the precipitate was collected (3·9 g.). It crystallized from alcohol in prisms melting at 266–67° (Zemplen, *et al.*[9] quote m.p. 266° and 266–66·5°) (Found: C, 68·4; H, 4·7. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%). Acetylation by refluxing with pyridine and acetic anhydride gave the acetyl derivative, which crystallized from alcohol in flat needles, m.p. 184° (Found: C, 67·3; H, 5·0. $C_{19}H_{16}O_6$ requires C, 67·1; H, 4·7%).

Prunetin (I)

4′-Hydroxy-5: 7-dimethoxyisoflavone (0·2 g.) was added to a solution of anhydrous aluminium chloride (0·2 g.) in nitrobenzene (2 c.c.), and heated on a boiling water-bath for one hour. The mixture was cooled and treated with dilute hydrochloric acid and ether. The ether layer was washed thrice with dilute hydrochloric acid, then with water and finally extracted with 1% aqueous caustic soda. A purple solution was obtained. On acidifying the alkaline extract, a colourless precipitate (0·11 g.) was obtained. It crystallized from dilute alcohol in needles, m.p. 237–38° (Found: C, 67·7; H, 4·5. $C_{16}H_{12}O_5$ requires C, 67·6; H, 4·2%). An alcoholic solution of the substance gives with alcoholic ferric chloride a brown-violet colour which changes to dirty green on the addition of excess of reagent. On

acetylation with acetic anhydride and pyridine and crystallizing the product successively from dilute acetic acid and alcohol-acetic acid, the *acetyl* derivative was obtained in colourless plates m.p. 220–22° (Found: C, 64·8; H, 4·5. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·3%). The melting points quoted by Finnemore are 242° (corr.) for prunetin and 224–26° (corr.) for the diacetyl derivative. Chakravarti and Bhar record m.p. 237-38° for prunusetin and m.p. 220–22° for the diacetyl derivative. The melting points of our synthetic 5:4′-dihydroxy-7-methoxyisoflavone and its diacetyl derivative were not depressed by admixture with prunusetin and its diacetyl derivative respectively. Chakravarti and Bhar observed that prunusetin gave a brown-violet colour with ferric chloride, while Seshadri and Narasimhachari have not recorded the ferric reaction. We find that prunusetin exhibits the same ferric chloride coloration (brown-violet with a trace of the reagent and dirty green with further addition) as synthetic (I).

7-Hydroxyisoflavone

Benzyl 2:4-dihydroxyphenyl ketone (0·5 g.)[16] in freshly distilled ethyl formate (15 c.c.) was gradually added to finely pulverised sodium (0·5 g.). A vigorous reaction took place which was complete in about 4 hours. The mixture which was first light yellow, then deep yellow, orange-brown and finally brown, was cautiously poured into ice and dilute hydrochloric acid. A brownish-yellow semi-solid mass, which soon solidified, separated. This was filtered, dried and dissolved in concentrated sulphuric acid (15 c.c.). After 3 hours the sulphuric acid solution was poured over crushed ice. The brown precipitate crystallized from dilute alcohol in white plates (0·25 g.), m.p. 210°. No depression in the m.p. was observed when mixed with a sample of 7-hydroxyisoflavone prepared earlier from 4-benzyloxy-2-hydroxyphenyl benzyl ketone.

Benzyl 2-hydroxy-4:6-dimethoxyphenyl ketone (XIII)

Benzyl 2:4:6-trihydroxyphenyl ketone (2·45 g.)[16] was refluxed with dry acetone (30 c.c.), freshly ignited potassium carbonate (4 g.) and dimethyl sulphate (2·5 g., 2 mols.) for 14 hours. The product was poured into water, excess acetone removed on the water-bath, the precipitate collected and crystallized from alcohol. The colourless square plates (1·85 g.) melted at 116° (Found: C, 70·5; H, 5·7. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%). The alcoholic solution gives a wine-red colour with ferric chloride.

5:7-Dimethoxyisoflavone (XIV)

Benzyl 2-hydroxy-4:6-dimethoxyphenyl ketone (1 g.), dissolved in freshly distilled ethyl formate (24 c.c.), was gradually added to finely divided

sodium (1 g.). There was at first a very slow reaction, but soon it became vigorous. In 4 hours the sodium went completely into solution. The light reddish brown reaction product was added to ice and dilute hydrochloric acid, and excess ethyl formate allowed to evaporate off. The sticky solid was filtered, dried and dissolved in concentrated sulphuric acid (10 c.c.). After 4 hours the sulphuric acid solution was poured over crushed ice and the grey solid filtered off and crystallized twice from dilute alcohol. The white plates (0·5 g.) melted at 120° (Found: C, 72·7; H, 4·7. $C_{17}H_{14}O_4$ requires C, 72·3; H, 4·9%).

5-Hydroxy-7-methoxyisoflavone (*XV*)

5:7-Dimethoxyisoflavone (0·2 g.) was dissolved in acetic anhydride (2 c.c.) and hydrobromic acid (d., 1·5; 2 c.c.). The mixture was refluxed for 6 hours. The reaction product was poured into water and the precipitate which separated was collected. It crystallized from 50% alcohol in elongated plates, which melted at 139–40° (Found: C, 72·0; H, 4·1. $C_{16}H_{12}O_4$ requires C, 71·6; H, 4·5%). The colourless alcoholic solution turns pale yellow when aqueous caustic soda is added and brown when aqueous ferric chloride is added.

5:7-Dihydroxyisoflavone (*XI*)

5:7-Dimethoxyisoflavone (0·15 g.) was added to hydriodic acid (d., 1·7; 1 c.c.), acetic anhydride (1 c.c.) and glacial acetic acid (1 c.c.). The mixture was refluxed for 4 hours, cooled, diluted with water and treated with sodium sulphite to destroy free iodine. The precipitate was collected, and crystallized from dilute alcohol. The colourless needles had m.p. 193–94° (Found: C, 70·8; H, 3·9. $C_{15}H_{10}O_4$ requires C, 70·9; H, 3·9%). The alcoholic solution of the substance gives a violet colour with ferric chloride; the solution in aqueous caustic soda is yellow. By refluxing the compound with acetic anhydride and a drop of pyridine 5:7-diacetoxyisoflavone was obtained. It crystallized from alcohol in white hairy needles melting at 180° (Found: C, 67·0; H, 4·1. $C_{19}H_{14}O_6$ requires C, 67·5; H, 4·1%).

4-Aminobenzyl 2:4:6-trihydroxyphenyl ketone (*XVI*)

Method (1).—A mixture of dry phloroglucinol (2 g.), *p*-acetamidobenzyl cyanide (2 g.),[17] dry ether (30 c.c.) and powdered fused zinc chloride (1 g.) was cooled in ice, and a stream of dry hydrogen chloride passed for 4 hours. It was then left in the refrigerator for 4 days. Ether was decanted off from the yellowish brown ketimine hydrochloride, and the latter once washed with ether. It was then added to water (100 c.c.), and the aqueous mixture refluxed for 2 hours, filtered and cooled. The solid that separated

was treated with sodium bicarbonate, and the product thus obtained crystallized from dilute alcohol. The pale yellowish plates melted at 197° (Found: N, 5·0. $C_{14}H_{13}O_4N$ requires N, 5·4%). The alcoholic solution gives a violet brown colour with ferric chloride. A crystalline precipitate of the hydrochloride is obtained on addition of hydrochloric acid. On cooling the acid solution in ice and adding sodium nitrite, a deep yellow solution is obtained, which couples with alkaline β-naphthol to a deep red dye. An orange-yellow precipitate gradually separates from the diazonium solution.

Method (2).—2 : 4 : 6-Trihydroxyphenyl-4-nitrobenzyl ketone (1 g.) was dissolved in alcohol (60 c.c.) containing Raney nickel catalyst (1 g.), and shaken in a Parr hydrogenator with hydrogen at 40 lb. pressure for 6 hours. The reaction product was filtered, the catalyst washed with alcohol and the filtrate diluted with water after removing the major portion of alcohol on the water-bath. A precipitate (0·6 g.) was obtained. It crystallized from alcohol in yellow plates melting at 190°. No depression in the melting point was observed when mixed with the compound obtained by method (1).

4-Aminobenzyl 2-hydroxy-4 : 6-dimethoxyphenyl ketone (XVII)

2-Hydroxy-4 : 6-dimethoxyphenyl 4-nitrobenzyl ketone (2 g.) was suspended in alcohol (50 c.c.) containing Raney nickel catalyst (2 g.) and shaken in a Parr hydrogenator with hydrogen at 40 lb. pressure for 8 hours. The reaction mixture was filtered, the catalyst washed with alcohol and the filtrate diluted with water after removing the major portion of alcohol by distillation. The pale brown precipitate crystallized from dilute alcohol in yellow needles, m.p. 103–04° (Found: N, 5·4. $C_{16}H_{17}O_4N$ requires N, 4·9%). The substance gives a brown coloration with alcoholic ferric chloride. It dissolves in hot dilute hydrochloric acid, and on cooling the solution the amine hydrochloride separates in needles melting at 198–200° (Found: N, 3·8. $C_{16}H_{18}O_4NCl$ requires N, 4·3%).

4-Acetamidobenzyl 2-hydroxy-4 : 6-dimethoxyphenyl ketone (XVIII)

4-Aminobenzyl 2-hydroxy-4 : 6-dimethoxyphenyl ketone (0·1 g.) was dissolved in hot toluene (2 c.c.) and cooled. A drop of acetyl chloride was added when a white crystalline precipitate separated immediately. After 10 minutes the precipitate was collected and crystallized from alcohol. The colourless needles melted at 159–60° (Found: N, 4·5. $C_{18}H_{19}O_5N$ requires N, 4·2%). The substance is insoluble in hot dilute hydrochloric acid. The alcoholic solution gives a violet brown colour with ferric chloride.

4-Hydroxybenzyl 2-hydroxy-4: 6-dimethoxy phenyl ketone (XIX)

The hydrochloride of the amine (XVII) (2·75 g.) was suspended in a mixture of concentrated sulphuric acid (8 c.c.) and water (80 c.c.) in a 250 c.c. three-necked flask fitted with a thermometer, dropping funnel and condenser. The contents were heated to boiling; when the amine hydrochloride completely went into solution, sodium nitrite (0·68 g., 1 mol.) in water (7 c.c.) was added dropwise in the course of 10 minutes. There was a vigorous reaction and the mixture became reddish-brown with a dark oil floating on the top. When the addition of sodium nitrite was over, water (15 c.c.) was added and the mixture heated to boiling, and then cooled. The flask was left overnight at room temperature. The dark solid was filtered off, taken up in hot alcohol and cooled. The alcoholic solution was filtered and evaporated to dryness on a water-bath. The residue was extracted four times with 25 c.c. portions of ether. The yellow ether solution was treated with norit, filtered and the ether removed by evaporation. The yellow residue (0·8 g.) melted at 98° with previous shrinking. On crystallizing from dilute alcohol it separated in needles melting at 110°. No depression in the m.p. was observed when the compound was mixed with a sample of 4-hydroxybenzyl 2-hydroxy-4: 6-dimethoxyphenyl ketone, prepared according to Zemplen and Bognar, who quote the m.p. 112° (corr.)[9] (Found: C, 66·4; H, 5·7. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%).

Summary

A synthesis of the naturally occurring isoflavone prunetin (5: 4′-dihydroxy-7-methoxyisoflavone) is described. 5: 7-Dimethoxy-4′-nitroisoflavone (IX) was prepared by the action of ethyl orthoformate, pyridine and piperidine on 2-hydroxy-4: 6-dimethoxyphenyl 4-nitrobenzyl ketone. The nitro compound was reduced to the amine, which was diazotized and boiled with sulphuric acid. 4′-Hydroxy-5: 7-dimethoxyisoflavone thus obtained was demethylated in the 5-position by means of aluminium chloride in nitrobenzene. The product, 5: 4′-dihydroxy-7-methoxyisoflavone agreed in all its properties with prunetin, as well as prunusetin. The latter, isolated by Chakravarti from *Prunus puddum*, is therefore identical with prunetin.

7-Hydroxyisoflavone can be prepared by the action of sodium and ethyl formate on benzyl 2: 4-dihydroxyphenyl ketone, protection of the 4-hydroxyl group not being necessary; but under the same conditions of reaction 5: 7-dihydroxyisoflavone was not obtainable from benzyl 2: 4: 6-trihydroxyphenyl ketone. Partial methylation of the latter to benzyl 2-hydroxy-4: 6-dimethoxyphenyl ketone, followed by treatment with sodium and ethyl formate, led readily to 5: 7-dimethoxyisoflavone. Demethylation with

hydriodic acid gave 5:7-dihydroxyisoflavone, while the action of hydrobromic acid in acetic acid yielded 5-hydroxy-7-methoxyisoflavone.

ACKNOWLEDGMENT

Our thanks are due to Mr. T. S. Gore, B.Sc. (TECH.), for carrying out the microanalyses recorded in the paper. We are greatly indebted to Dr. D. Chakravarti and Professor T. R. Seshadri for samples of prunusetin and its acetyl derivative.

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TEMPERATURE DEPENDENCE OF ULTRASONIC VELOCITY IN ALCOHOLS

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Received December, 25, 1950

(Communicated by Prof. S. Bhagavantam, F.A.SC.)

I. Introduction

The change of ultrasonic velocity in water with temperature has in recent years been investigated by Jones and Gale (1946) and Willard (1947). They made use of the sonic interferometer and showed that the velocity increases with temperature up to a maximum and then decreases. The temperature corresponding to the maximum velocity is at about 74° C. So far only water is known to behave in this peculiar manner and it can be attributed to the association of its molecules. There is a good deal of evidence to show that the molecules of water have a tendency to form clusters and that these clusters progressively break up at higher temperatures causing the compressibility to decrease. This brings about an increase in the ultrasonic velocity.

It is known that the paraffin alcohols also show association. The ultrasonic velocity in a few of these has been determined at room temperatures or near about by a number of workers (Parthasarathy, 1935; Rendall, 1943; Willard, 1947; Burton, 1948). Although it is known that the temperature coefficient of velocity in them at these temperatures is negative, unlike that in water, their general behaviour up to the boiling point has not been studied. In the present work an accurate arrangement for controlling the temperature and measuring the ultrasonic velocity has been set up, in another connection, and it is used for verifying the peculiar behaviour reported in water and for ascertaining how far the alcohols resemble water in this respect.

II. Experimental Arrangements and Results

The cell containing the liquid was placed in a water thermostat, the temperature of which could be kept constant to within 1/10 degree centigrade. The diffraction patterns, with the usual arrangement, were photographed and the distance between the orders measured on a Hilger Comparator. After completing one alcohol, a comparison photograph of water

was taken. From the known value of the velocity in water, the velocity in the alcohol was calculated.

The waves in the liquid were generated by exciting an X-cut quartz crystal to vibrate at one of its harmonics. The frequency used was 4·5 Megacycles per second. For all liquids the frequency was the same, and the constancy of this was checked from time to time by a heterodyne method.

Water, methyl, ethyl, isopropyl, tertiary butyl and normal amyl alcohols were investigated. The results in water agree very closely with those reported by the workers already referred to and are not therefore given here. Results, in respect of other liquids, are given in the following tables: Fig. 1 shows

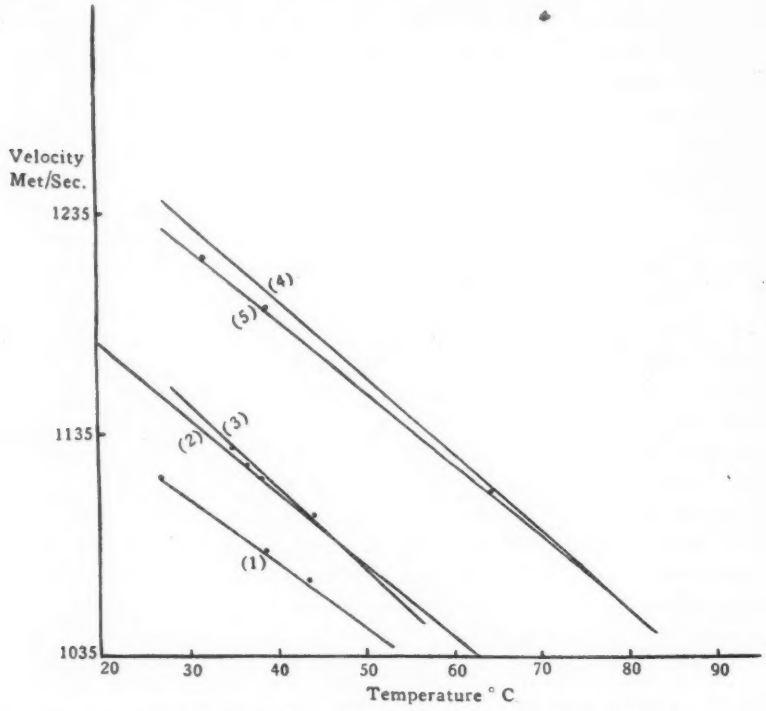

FIG. 1. Methyl Alcohol, 2 Ethyl Alcohol, 3. Iso-Propyl Alcohol, 4. Tertiary Butyl Alcohol, 5. Normal Amyl Alcohol.

graphically the nature of the variation. They all differ from water in that the velocity decreases with increasing temperature. The association in alcohols is obviously of a kind different from that obtained in water. It is

:nteresting to note that the graph is nearly a straight line with a gradient of about 3 meters per second per degree in every case.

Liquid	θ°C.	V Metres/sec.	Liquid	θ°C.	V Meters/sec.
Methyl Alcohol	27·0	1118	Tertiary Butyl Alcohol	27·5	1241
	31·5	1099		33·5	1217
	38·5	1082		38·0	1203
	43·5	1069		44·0	1188
	48·5	1052		47·0	1169
	52·5	1043		50·5	1157
				55·5	1139
Ethyl Alcohol	20·0	1180		60·0	1124
	30·0	1142		74·5	1081
	33·5	1131		80·0	1059
	36·5	1122			
	39·0	1113	Normal Amyl Alcohol	27·5	1229
	44·0	1098		31·5	1214
	50·0	1076		38·5	1192
	54·5	1061		46·5	1167
	59·0	1046		53·0	1139
				57·5	1126
Iso-propyl Alcohol	28·0	1157		64·0	1109
	35·0	1129		68·0	1093
	44·0	1098		74·0	1074
	50·0	1074		78·5	1069
	56·5	1050		82·5	1052

θ = Temperature V = Velocity

In ccnclusion, the author wishes to express his thankfulness to Prof. S. Bhagavantam for his helpful guidance in the course of this work.

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124-81 Printed at The Bangalore Press, Bangalore City, by G. Srinivasa Rao, Superintendent
and Published by The Indian Academy of Sciences, Bangalore